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AIDS
TO
PHYSIOLOGY

BY

HENRY DRYERRE
PH.D., M.R.C.S., L.R.C.P.(LOND.), F.R.S.E.
PROFESSOR OF PHYSIOLOGY, ROYAL (DICK) VETERINARY COLLEGE
LATE LECTURER IN PHYSIOLOGY, UNIVERSITY, EDINBURGH;
EXAMINER IN PHYSIOLOGY FOR ROYAL COLLEGE OF
SURGEONS, EDINBURGH, UNIVERSITY OF GLASGOW
AND PHARMACEUTICAL SOCIETY OF GREAT BRITAIN

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AIDS TO PHYSIOLOGY

CHAPTER I

INTRODUCTORY—THE CELL AND CELL DIVISION

Physiology deals with the manner in which the organs and tissues of the body perform their functions. The forces of physics and chemistry play a very important part in the performance of these functions. The object of the physiologist is as far as possible to refer these functions to their ultimate chemical or physical explanation.

Living matter or **protoplasm** shows the following phenomena:

1. **Irritability**—the property of responding in a particular way to the application of a stimulus.
2. **Metabolism**—under which we include all the chemical changes produced during activity. Food materials are built up into higher complexes (**Anabolism**). On the other hand, complex molecules already built up are disintegrated (**Katabolism**), and effete products got rid of (**Excretion**). **Respiration** is gaseous metabolism.
3. **Growth.**
4. **Reproduction.**

The Animal Cell.

Cells are the microscopic elements of structure from which the other tissues are ultimately formed, either by the modification of the cells themselves or by the formation of an intercellular matrix.

The cell consists of a mass of **protoplasm,** which is differentiated into a **nucleus** with surrounding **cytoplasm.** The nucleus consists essentially of two parts:

1. A formed material of a viscous nature called **chromatin** disposed both as an internal **network** and as the **nuclear membrane.** This chromatin is composed of nuclein, a combination of nucleic acid with protein. In dividing cells the nuclear membrane disappears.
2. The **karyoplasm,** clear and structureless, occupying the meshes of the network.

Within the nucleus there may also be one or more globular bodies—**nucleoli.** Those which stain with basic dyes are known as **karyosomes,** those which have an affinity for acidic dyes are called **plasmosomes.**

The cytoplasm in the living cell is devoid of structure. In it there may be pigment granules, fat globules, glycogen granules, and vacuoles containing fluid. In the cytoplasm of many cells a special structure, the **centrosome,** is found. This appears as a radiating structure surrounding a small particle, the centriole. The centrosome is especially involved in cell division.

Mitochondria and the apparatus of **Golgi** are also present. These are filamentous or reticular bodies composed of proteins and lipides, and are believed to be intimately connected with the metabolic activities of the cell.

Cell Division.

Every cell is developed from a pre-existing cell usually by division into two parts. The origin of a cell from anything but a cell is as unknown as the origin of an animal or plant from anything but a parent animal or plant.

The division of the cell is preceded by the division of its nucleus, directly—that is, by the immediate splitting of the nucleus into two parts; or indirectly—that is, by the nucleus undergoing a series of changes

known as **karyokinesis.** Indirect nuclear division is now recognised as being the more usual process.

Briefly, karyokinesis consists of events taking place in the following order:

1. The centrosome divides into two, and these migrate to opposite poles of the cell.
2. The chromatin filaments, the nuclear membrane and the nucleoli combine to form a continuous filament.
3. This filament breaks into segments (**chromosomes**). (The number of chromosomes is always the same for each species, and in man they number forty-eight.)
4. These chromosomes assume a **V** shape, and arrange themselves in the form of a rosette—the **aster** phase.
5. Each chromosome now splits longitudinally, their number thus being doubled.
6. The split portions move to opposite poles and arrange themselves radially around the centrosomes, forming two stars—the **diaster** phase.
7. The chromosomes join up into a continuous skein, nuclear membranes appear, and two nuclei are formed.

The protoplasm of the cell then divides by constriction, and two cells are thus produced.

In the higher animals the cells which differentiate to form the reproductive elements at first also undergo the ordinary karyokinetic changes, but later undergo meiotic division (heterotypical mitosis), in which the resulting daughter-cells contain only half the normal number of chromosomes.

Amœboid Movement.

Many cells, such as amœbæ, leucocytes, etc., exhibit flowing movements, which are apparently spontaneous. Seeing, however, that similar movements may be produced in oil-drops floating in water to which a trace of alkali has been added (which locally reduces the surface-tension of the oil-drop),

it has been concluded that amœboid movements are due to alterations in surface-tension. Movement occurs by the protoplasm being attracted (positive) or repelled (negative) by certain physical or chemical stimuli—thermotaxis, phototaxis, or chemiotaxis.

Intake of Foreign Particles.

Cells that have the power of amœboid movement frequently engulf or ingest formed particles, such as Indian ink, carmine grains, or bacteria. The process is often termed phagocytosis, though the same term is also used to include subsequent digestion of the ingested matter.

CHAPTER II

THE CHEMISTRY OF THE BODY

The following elements enter into the composition of all living organisms, C, H, O, N, S, P, Cl, K, Na, Ca, Mg and Fe; also small amounts of F and I in some.

These elements are present mainly in combination—for example, water; chlorides of sodium and potassium (body fluids); phosphates and carbonates of calcium and magnesium (in bone); carbonates and bicarbonates of the various alkalies (body fluids); sulphates also occur. Fluorine is found in teeth and bones, and iodine in the thyroid secretion. Water, which forms about 70 per cent. of the body, is present in all the tissues. There is less than 0·5 per cent. in the enamel of the teeth, whilst organs like muscle, lungs, etc., contain about 75 per cent.

The numerous proximate principles of which the body consists belong to or are derived from three main classes: (1) **Lipides**; (2) **Carbohydrates**; (3) **Proteins.**

Lipides.

These are substances containing esters of fatty acids; they are all insoluble in water, but dissolve in chloroform, benzene and ether. They may be (*a*) **simple,** (*b*) **compound,** (*c*) **derived.**

(*a*) Simple—esters of fatty acids with alcohols These are called:
Fats, if the alcohol is glycerol.
Waxes, if the alcohol is other than glycerol.

(*b*) Compound—esters of fatty acids containing substances in addition to an alcohol. Two groups are well known:
Phosphatides, substituted fats, containing H_3PO_4 and N—*e.g.*, lecithin, cephalin.
Glycolipides, compounds of fats with galactose and N, but *no* H_3PO_4,—*e.g.*, cerebrosides.

(*c*) Derived—obtained from above by hydrolysis, they are fatty acids and sterols. The latter are mostly alcohols of high molecular weight —*e.g.*, **cholesterol.**

Fats are colourless and contain only C, H and O, and as already stated are combinations of fatty acids with glycerol. Glycerol is tri-basic, and can combine with three molecules of the monovalent fatty acids. These esters are sometimes termed **glycerides,** and are named after the acids from which they are formed —*e.g.*, tripalmitin is the glyceride of palmitic acid. Its structure may be schematically represented as follows:

Glycerol < Palmitic acid.
Palmitic acid.
Palmitic acid.

The combination of these is represented by the following formula:

$$C_3H_5(OH)_3 + 3C_{15}H_{31}COOH = C_3H_5(C_{15}H_{31}COO)_3 + 3H_2O.$$

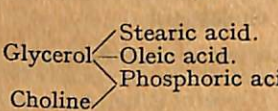
It will be observed that three molecules of water are liberated in this reaction. When fats are acted upon

by superheated steam, the water again enters into the compound, and splits it up into glycerol and fatty acid. A neutral fat when boiled with an alkali (*e.g.*, NaOH) forms an alkali salt of the fatty acid (a soap), and glycerol is liberated. This is known as **saponification.**

The fatty acids most commonly found in the body are palmitic ($C_{15}H_{31}COOH$), stearic ($C_{17}H_{35}COOH$), and oleic ($C_{17}H_{33}COOH$). The first two are solid and the third is liquid. It should be noted that all the naturally occurring fatty acids have an even number of carbon atoms in the molecule.

Fat mixtures containing a large proportion of tristearin and tripalmitin are solid at ordinary temperatures; on the other hand, if a relatively large amount of triolein be present, they are soft or even liquid. Fats are found in adipose tissue, milk, and white bone-marrow.

Lecithin is found in the yolk of eggs, in nerve tissue, etc. Its structure may be represented as follows:



Cholesterol, a secondary alcohol, is found in bile, blood, milk, yolk of egg, and in other animal tissues.

Carbohydrates.

These are naturally occurring substances, composed of C, H, and O, in which the ratio of H to O is the same as in water. Physiologically they form an important group, which includes the sugars.

The known sugars consist of chains of from three to ten C atoms (trioses, tetroses, pentoses, hexoses, etc.).

The hexoses are the most important sugars, and are divided into three groups:

(1) Monosaccharides—
e.g., glucose and fructose ($C_6H_{12}O_6$).

(2) Disaccharides—
e.g., maltose and cane-sugar ($2C_6H_{12}O_6 - H_2O$).
(3) Polysaccharides—
e.g., starch and dextrin ($nC_6H_{12}O_6 - (n-1)H_2O$).

Only glucose, fructose, mannose, and galactose of all the hexoses are assimilable by the animal organism. The following reactions are of importance:

(*a*) **Reduction.**—All the monosaccharides are strong reducing agents. A number of tests are based upon this fact. **Trommer's test**: a solution of caustic soda is added to the liquid to be tested, and then a drop or two of copper sulphate solution. The blue solution which is thus produced is now boiled; a yellow and a yellow-red precipitate of cuprous oxide are formed. This test may be carried out with Fehling's solution, which is an alkaline solution of cupric hydrate in Rochelle salt, or by using Benedict's solution.

(*b*) **Osazone** crystals of characteristic shape are formed when the monosaccharides are combined with phenylhydrazine.

(*c*) **Optical Activity.**—The sugars show different degrees of rotation. The instrument required to measure the degree of rotation is called a polarimeter or saccharimeter. Glucose is dextrorotatory; its specific rotation is 52·7° in 10 per cent. aqueous solution. Fructose is lævorotatory; its specific rotation is 93°. Lactose is dextrorotatory; its specific rotation is 52·5°.

(*d*) **Fermentation** with yeast, and the formation of alcohol and CO_2.

Cane-sugar (sp. rot. + 66·5) is rapidly hydrolysed by boiling with dilute acids. This process is called inversion, because the dextrorotatory cane-sugar solution has become lævorotatory —20 (inverted rotation) owing to it having been converted into a mixture of glucose and fructose (invert sugar).

Glycogen or animal starch, which is found in the

liver, muscles, and other tissues, gives a reddish-brown colour with iodine (destroyed by boiling, but reappearing on cooling).

When starches are hydrolysed with weak acids the first products are dextrins, of which the two most important are erythrodextrin (red dextrin—red colour with iodine) and achroödextrin (colourless—no colour with iodine solution).

Proteins.

This is a large class of substances which possess the common trait of being compounded of numerous different amino-acids. These amino-acids are known as the foundation-stones or units of the protein molecule. They are important in that they all contain nitrogen in their composition, and, in addition, may possess an aromatic nucleus.

Proteins contain C, H, O, and N, and generally also S (cystine). In some P and I are also present.

Proteins can be broken up into their units by means of concentrated H_2SO_4, HCl, or alkalies. Certain proteins can also be split up by ferments (proteases). In the hydrolysis of proteins four stages can be made out, viz.—

(1) Acid or Alkali metaproteins.
(2) Proteoses and peptones (most likely only mixtures of various polypeptides).
(3) Polypeptides (three or more amino-acids grouped together).
(4) Amino-acids.

Tests for Proteins.—The main tests are colour reactions and precipitation reactions.

1. **Colour Reactions:**

(1) The solution is made alkaline with NaOH or KOH solution, and, a drop of weak copper sulphate solution added, a violet colour is produced due to the presence of two CO—NH_2 groups in the protein molecule (Biuret test).

Other colour reactions depend upon the presence of an aromatic ring in the protein molecule:

(2) To the solution is added some concentrated HNO_3; a white precipitate forms, which becomes yellow on heating. When, after cooling, an alkali is added, an **orange** colour is produced (xanthoproteic test).
(3) A solution of mercurous and mercuric nitrates (Millon's reagent) gives a white precipitate, which on heating becomes brick red. This reaction depends upon the presence of tyrosine.
(4) The aromatic radical tryptophan gives with glyoxylic acid and sulphuric acid a blue violet colour (Hopkins' modification of the Adamkiewicz reaction).
(5) A protein with loosely combined sulphur will give a black precipitate with lead acetate and caustic alkali.

2. **Precipitation Reactions:**

(1) Precipitation with alcohol.
(2) Salting out with large quantities of neutral salts. The salts most commonly used are Na_2SO_4, NaCl, $MgSO_4$ and $(NH_4)_2SO_4$.
(3) Precipitation by strong mineral acids—*e.g.*, HNO_3 (Heller's test).
(4) Coagulation and precipitation by heat. For this reaction the solution must be slightly but definitely acid.
(5) Precipitation by means of other colloids (adsorption)—*e.g.*, dialysed iron.
(6) Precipitation by the heavy metals—*e.g.*, $HgCl_2$, $CuSO_4$.

Classification.—Proteins cannot at present be grouped in terms of their chemical composition. They may, however, be subdivided into the following classes:

1. **Albumins.**—Soluble in water and in dilute neutral saline solutions. Not precipitated by means of acids or alkalies in watery solution. Precipitated, however, from salt-rich solutions (NaCl, $MgSO_4$) by means

of small quantities of acids. Coagulate on boiling only in presence of salts. Precipitated by saturating their solutions with $(NH_4)_2SO_4$. They have a high sulphur content. Examples are serum-albumin, lact-albumin, and egg-albumin.

2. **Globulins.**—Insoluble in pure water, but soluble in dilute neutral salt solutions. They are coagulated by heat; they are readily salted out of their solutions; they do not crystallise. Examples are serum-globulin, fibrinogen, thyreoglobulin.

3. **Sclero-Proteins.**—This group contains most of the substances which were once known as albuminoids. They form the principal constituents of the skeletal tissues and connective tissues, as well as of hairs, etc. They are characterised by great insolubility in all neutral solvents. Examples are stromin, collagen, elastin, and keratin.

4. **Phospho-Proteins.**—They contain phosphoric acid —*e.g.*, caseinogen and vitellin.

5. **Protamines.**—Present only in the heads of spermatozoa of some fishes, and called, accordingly, salmine, sturine, etc. They give the Biuret test, but generally fail to give Millon's reaction. Arginine is obtained when some of them are hydrolysed.

6. **Histones.**—Found in red blood corpuscles, the protein moiety in hæmoglobin (globin). They coagulate by heat, and are soluble in dilute acids.

7. **Conjugated Proteins.**—

(*a*) Chromo-Proteins.—The protein is here united to a pigment—*e.g.*, hæmoglobin. The pigment usually contains Fe.

(*b*) Glyco-Proteins.—Here a carbohydrate group is compounded with the protein. The carbohydrate is not a sugar, but a nitrogenous substance—glucosamine—which has reducing properties similar to sugar. Examples are mucin, chondro-mucoid, and ovo-mucoid.

(*c*) Nucleo-Proteins.—Are constituents of cell nuclei. The protein is combined with nucleic acid. The nucleic acid consists of phosphoric acid united by means of a carbo-

hydrate group to a nitrogenous base, which latter consists of purine bodies and pyrimidine derivatives.

Proteins, because of the large molecules of which they are composed, form colloidal solutions. A colloidal solution is intermediate between a true solution and a suspension of fine particles in water. A colloid does not pass so readily through an animal membrane as a crystalloid, neither does it crystallise readily, although many colloids have now been obtained in a crystalline form.

Colloids when they are in solution form **sols**; when the solvent is water they are called **hydrosols**; when alcohol, alcosols. Colloids have also a more solid form, known as a jelly or **gel**; this can be produced by means of physical and chemical changes, equivalent to those that would cause a crystallisation of crystalloids—*e.g.*, cooling, dehydration, etc.

The particles of a substance forming a colloidal solution may be aggregated together and precipitated by heat, or by mechanical means (shaking), or by the addition of certain salts. This process is known as **coagulation.** Gels, because of the large surface which they present, have the power of taking up other substances from solution; this is known as **adsorption.**

Proteins when treated with alkaline salts form gels, but with salts of the heavy metals or with heat they are coagulated and precipitated.

CHAPTER III

CONNECTIVE TISSUES AND EPITHELIA

The Histology of the Tissues.

The textures of which the living body is built are called **tissues.** The investigation of their microscopic structure constitutes the science of **Histology.**

There are four chief kinds of tissue—viz., **con-**

nective, epithelial, muscular, and **nervous.** Most organs are formed of more than one tissue, the connective tissues especially being very widely distributed and forming part of almost every organ.

Cells enter into the composition of every tissue. As a rule they are separated by **intercellular substance,** which stains with silver nitrate; but in some cases the cells are in complete continuity, and form a **syncytium** (*e.g.*, heart muscle). Where the intercellular material is small in amount, it is called **cement substance;** when abundant, it is called **matrix** or **ground substance.**

The Connective Tissues.

The connective tissues are all mesoblastic in origin, and include areolar, fibrous, and elastic tissue; reticular (retiform) and lymphoid (adenoid) tissue; adipose tissue; cartilage and bone. They exhibit the following characters:

They consist of **cells** embedded in an intercellular substance, the **matrix.** The **intercellular substance** is usually abundant; it may be transparent and without obvious structure (hyaline), or fibrous, or even impregnated with earthy salts, as in bone. In other cases it is fluid, or nearly fluid. The matrix consists of a protein or protein-like material, and yields either **mucin, gelatin,** or some allied substance.

The fibres of the matrix in the connective tissues are of two kinds: **white fibres,** or white bands, consisting of **collagen,** which easily become converted into gelatin by boiling, and which swell, become transparent, and ultimately dissolve even in very dilute acetic acid; and **yellow elastic fibres,** which are at first unaltered by boiling, but eventually yield a substance known as **elastin**: they resist the action of dilute acids and alkalies. Yellow fibres consist of elastin. Both yellow and white fibres are either formed from cells in the embryo, or, as some believe, are produced by fibrillation of a homogeneous matrix; in either case they bear the same relation to the permanent cells, in the fibrous connective tissues, that the matrix does in cartilage and bone.

Areolar Tissue (familiar as the material that is cleaned off muscles in dissecting) is at once the most widely diffused and the most generalised of all the connective tissues. The matrix is fluid and contains two kinds of fibres: (1) **white fibres,** consisting of extremely delicate parallel fibrils connected to form wavy bundles, which under tension become straight, but are relatively inextensible on further tension; (2) **elastic fibres,** running, not in bundles, but singly, and uniting with adjacent fibres by branching so as

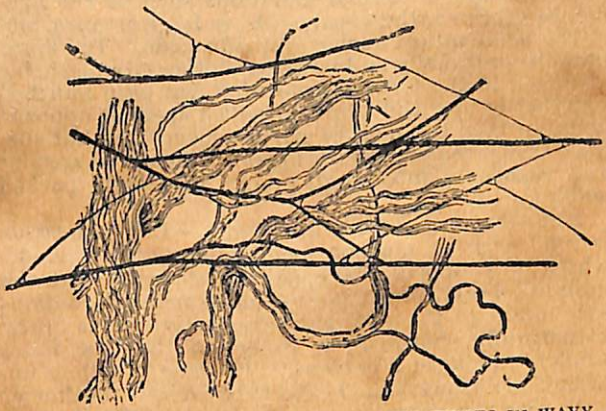


FIG. 1.—AREOLAR TISSUE, SHOWING WHITE FIBRES IN WAVY BUNDLES, AND ELASTIC FIBRES.

to form a network. White fibres are somewhat difficult to stain, but elastic fibres stain intensely with magenta and orcëin. Various cells (**connective-tissue corpuscles**) occur in areolar tissue: the chief are (1) flattened **lamellar cells,** (2) **mast cells** with basiphil granules, and (3) **wander-cells** with oxyphil granules. Many of the cells are branched.

Fibrous Tissue.—This form of tissue is found in fasciae, ligaments, tendons, and the various fibro-serous membranes of the body. It is almost inextensible, and exceedingly strong and tough. The bundles

of white filaments cohere very intimately, either running parallel, as in tendon, or intercrossing, as in some aponeuroses and in the dura mater. Elastic fibres are absent, and the cells, which are all of the lamellar variety, have their form impressed on them by the bundles betwixt which they lie. Thus, in tendon they are like short sections of a fluted column, appearing oblong in the direction of the tendon, and stellate on end-view.

ELASTIC TISSUE, consisting in great part of elastic fibres, occurs in special situations such as the ligamenta subflava, the vocal cords, in large arteries, and in the ligamentum nuchæ of quadrupeds. The fibres branch continually and unite with other strands, being arranged in the form of a net that has been bunched together in one direction and pulled apart at opposite ends, so that the meshes are no longer open but slit-like. On cross-section the fibres are seen to be angular and separated into small groups by closely packed white fibres.

RETIFORM AND LYMPHOID TISSUE.—Retiform tissue is met with in mucous membranes and in glands, where it supports the epithelial elements and the vessels. Its chemical nature and its staining reactions are similar to those of white connective-tissue fibres. Structurally, however, it differs in that the fibres branch and form a network. In some situations unbranched fibrous tissue is seen to be directly continuous with retiform or reticular tissue, thus further proving the essential identity of the two. In lymph glands, Peyer's patches, etc., where the tissue supports lymphocytes, it is named **lymphoid** or **adenoid** tissue.

ADIPOSE TISSUE is virtually areolar tissue enclosing fat-cells. The protoplasm of these latter contains one or many globules of fat. These fat-cells may be so numerous as to obscure the enclosing areolar tissue. The fat may be stained with osmic acid, Scharlach R, or Sudan III.

All the preceding forms of connective tissue are obvious modifications of areolar tissue. In the succeeding two forms the primitive structure is more masked.

CARTILAGE.—In this material the cells are, generally speaking, rounded and devoid of branches. The matrix is not fluid, but firm and elastic: it is, however, transparent, and in one variety—the **hyaline**—it is devoid of fibres. When yellow elastic fibres are present in the matrix, the cartilage is called **elastic fibro-cartilage**; when white fibres are present, it is called **white fibro-cartilage.** Both these latter varieties may be recognised at once by the form of the cells. Blood and lymph vessels are very rare in cartilage. Cartilage is commonly known as **gristle.**

In **Hyaline Cartilage** the matrix is transparent or finely granular, forming concentric capsules around the cells. The cells are scattered in groups, and are more numerous in young subjects, where the cartilage is growing rapidly. Growth is effected by the multiplication of the cells, and when this takes place, chiefly in one direction, the cells become arranged in rows; this disposition arises from the division of the cells being most rapid in the direction of the most rapid growth.

Hyaline cartilage is spoken of as **temporary** when it is subsequently converted into bone; and **permanent** when it persists throughout life, or only becomes calcified by degeneration in old age. The permanent hyaline cartilages are those covering the ends of the bones in the more movable joints—**articular cartilages**—also the cartilages of the ribs, trachea and bronchi, nose, and the thyroid, cricoid, and arytenoid cartilages of the larynx.

The articular cartilages are distinguished by the arrangement of the cells in rows perpendicular to the surface of the cartilage, and by those on the free surface being flattened and possessing filamentous processes. The free surface of hyaline cartilage (articular excepted) is covered by a membrane richly supplied with blood vessels and nerves, called the **perichondrium.**

White Fibro-Cartilage, which occurs especially in the intervertebral discs, is exceedingly tough and strong. Under the microscope the wavy white fibres give the appearance of ordinary fibrous tissue; the

cells, however, being rounded, are immediately recognisable as cartilage cells.

Yellow Elastic Cartilage has a network of yellow elastic fibres in the matrix; it forms the cartilage of the external ear, Eustachian tube, the epiglottis, the cornicular and cuneiform cartilages of the larynx.

BONE consists of an earthy (hard and rigid) and an animal (tenacious and elastic) part intimately commingled. The earthy constituents, amounting to two-thirds of its weight, may be obtained by burning. The animal part, forming the remaining one-third, may be obtained by prolonged steeping in mineral acid, which dissolves the contained phosphate and carbonate of calcium. The decalcified bone retains every detail of the shape of the original, but is flexible and elastic. By other tests (*e.g.*, boiling) it is recognised that the animal matter, like fibrous tissue, is mainly composed of collagen. Sections of bone for microscopic examination may be prepared either by grinding the material into thin slices, or by decalcifying, cutting into sections, and staining.

The **cells of bone** are much smaller than those of cartilage. They lie in spaces in the matrix, called **lacunæ**, and send numerous fine branching processes throughout the matrix, which connect them with each other. The canals in which these processes lie are called **canaliculi.** Bone is vascular, and cartilage is either without vessels or almost without them. The vessels of the bone run in canals called **Haversian canals.**

The tissue of bone is either compact or cancellous. In the **compact** bone the arrangement of the Haversian canals is very regular, and the lacunæ are arranged in laminæ, forming cylinders around the Haversian canals. The **cancellous** bone is composed of thin plates forming a spongy tissue; there are either no Haversian canals in these plates, or very few, and the lacunæ are arranged in laminæ parallel with the surfaces of the plates.

Periosteum.—The bone is covered externally by the **periosteum,** which consists of two layers: an **external fibrous** layer, in which the vessels, nerves, and lymphatics of the bone ramify; and an **internal** layer, called

osteogenetic. This consists in young subjects of cells similar to colourless blood-corpuscles, from which the bone is developed, and the remains of which form the bone corpuscles of the lacunæ. These cells are called **osteoblasts.** After the bone ceases to grow, the osteogenetic layer becomes reduced to a single stratum of thin, flattened cells, resembling those of endothelium.

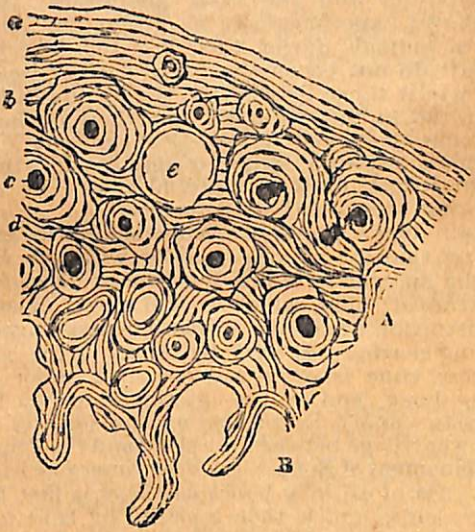


FIG. 2.—TRANSVERSE SECTION OF DECALCIFIED FEMUR OF CAT.

A, dense, B, spongy bone; *c*, Haversian canal; *a*, peripheral, *b*, Haversian, *d*, intermediate lamellæ; *e*, Haversian space.

Marrow.—The spaces of cancellous bone and the medullary cavities of the long bones are occupied by **marrow.** That in the shafts of the long bones, **white marrow,** consists chiefly of fat and closely resembles ordinary adipose tissue; that in the spaces of cancellous bone, **red marrow,** derives its name from its greater vascularity. It contains osteoblasts, osteoclasts and,

especially, developing erythrocytes and leucocytes. (See later under Blood, Chap. VI.) The supporting connective tissue is of the retiform variety.

Epiphyses.—The parts of the bone which are formed from secondary centres are called **epiphyses.** The increase in length takes place in the long bones by the growth of the cartilage (epiphyseal cartilage) between the epiphyses and the shaft (diaphysis); this has been shown experimentally by driving pegs into the bones of animals during their growth. The pegs in the shaft do not become removed further from each other, whilst those driven into the epiphyses become further and further removed from those in the shaft, as the consequence of the growth of the bone. Whenever the epiphyseal cartilage ossifies the growth of the bone in length ceases. Material injury by disease may bring this about prematurely.

Certain dyes have a remarkable affinity for growing bone, so that by mixing madder with the food of pigs, the manner in which the bone is deposited has been studied; that which is laid down during the administration of the dye is more or less tinged with colouring matter. It may be shown in this manner that new bone is deposited on the exterior of the growing bone, and in the interior of newly formed Haversian canals, as well as on the surfaces of the growing cartilage between the shaft and the epiphyses.

Development of Bone.—(1) *Bone formed in cartilage.* In the case of all long bones cartilage is first formed which calcifies and is then replaced by bone-forming cells in its interior along with layers of bone under the periosteum. (2) *Bone formed in membrane.* In this case there is no preliminary cartilage formation, only sub-periosteal ossification. Long bones are chiefly formed from cartilage; and most of the skull and face bones are formed from membrane.

The Regeneration of Bone.—In the adult, fractured bones are united by the formation of a callus due to the activity of the osteogenetic tissue on the inner layer of the periosteum, but in young animals the marrow cells appear also to participate in the process of repair.

The Epithelial Tissues.

Epithelium is composed entirely of cells with but little or no intercellular substance; it is generally found covering free surfaces, internal or external. The variety of epithelium that lines the serous and lymphatic cavities and the interior of the vascular system is often called endothelium, or even mesothelium to denote its origin from the mesoblast. All other varieties of epithelium are derived either from epiblast or from hypoblast.

The cells forming an epithelium may be only one layer deep or many layers deep. The latter arrangement is found especially in exposed situations. We distinguish the following varieties:

(i.) Pavement (ii.) Columnar	One layer deep.	
(iii.) Glandular, including goblet-cells (iv.) Ciliated		Usually one layer; may be more.
(v.) Stratified (vi.) Transitional	Many cells deep.	

(i.) PAVEMENT EPITHELIUM, which includes all endothelium, consists of very thin cells dovetailed together at their edges. The sinuous outlines of the cells are beautifully shown by means of silver nitrate, which stains the cement-material. Fine intercellular fibrils may often be seen connecting adjacent cells. Sites of occurrence: interior of vascular and lymphatic systems, anterior chamber of eye, alveoli of lungs, ducts of mammary glands.

(ii.) COLUMNAR EPITHELIUM.—The cells of this epithelium are **prismatic**; they extend from the cardiac extremity of the stomach to the rectum, and are also found lining the ducts of many glands. The free surface is usually thickened, so that in section it forms a border; this is striated in the direction of the axis of the cell; it is spoken of as the *striated border*. Columnar epithelium cells are usually long, but in some situations they appear cubical when seen in

profile. Such **cubical epithelium** lines the vesicles of the thyroid.

(iii.) GLANDULAR EPITHELIUM is found in the alveoli of the secreting glands. The cells, which are usually full of granules, are of various shapes. The granules are discharged during secretion. In the mucous salivary glands and in the fundic region of the stomach the secreting epithelium is two cells deep. **Goblet-cells** are mucus-secreting cells distended by the swelling up of their mucigen content. They are found most abundantly in the stomach and the large intestine.

(iv.) CILIATED EPITHELIUM.—The cells are usually

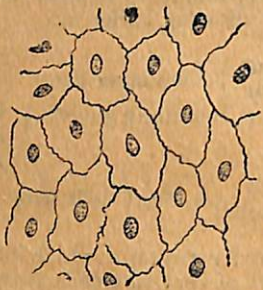


FIG. 3.—PAVEMENT EPITHELIUM OR ENDOTHELIUM OF FROGS' MESENTERY (SILVERED).

columnar, but may be cubical; the free surface of each cell is covered with very minute hair-like processes of protoplasm—**cilia**—which exhibit during life a continual vibratory movement. The combined lash-like movement of the cilia has been compared to the waves on a field of wheat when the wind blows over it. The to-and-fro movement occurs about ten times in a second. It continues when the cells are removed from the body and isolated from each other. It is not under the control of the nervous system, but apparently resembles the spontaneous movement of protoplasm. The vapour of chloroform, or carbon dioxide, stops ciliary action, and heat above 45° C.

immediately arrests this movement by the production of rigidity in the cilia.

Ciliated epithelium occurs in (1) the air-passages, (2) the uterus and Fallopian tubes, (3) the efferent ducts of the testis, (4) the ventricles of the brain and the spinal canal. In some of these places it exists as a simple layer; in other parts—*e.g.*, trachea—the ciliated layer rests upon deeper epithelial cells.

(v.) STRATIFIED EPITHELIUM.—The cells of this variety of epithelium form many layers, being **never**

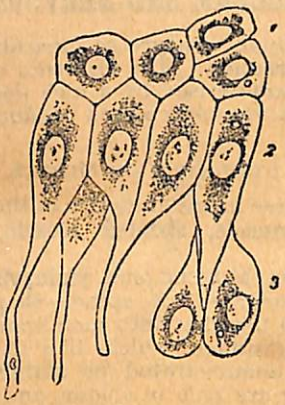


FIG. 4.—TRANSITIONAL EPITHELIUM FROM URINARY BLADDER. (RUTHERFORD.)

1, Cells at free surface; 2, cells in middle; 3, cells in deepest layer.

less than ten deep, more commonly fourteen. Those of the outer layers are flattened and scale-like, overlapping each other by their edges; those of the deeper layers are columnar. This form of epithelium covers the surface of the body, and lines the digestive tract from the lips to the lower end of the œsophagus (see also Epidermis, p. 138).

(vi.) TRANSITIONAL EPITHELIUM lines the urinary bladder and ureters. The cells, which are **three or**

four deep, vary in shape, being **pyriform, ovoid, spherical,** and **flattened,** and the layers are not so regularly arranged as in the stratified epithelium of the skin and œsophagus.

CHAPTER IV

THE MUSCULAR AND NERVOUS TISSUES

THE predominant feature of muscular tissue is its power of **contraction.** The elements of the nervous system are characterised by a high degree of **excitability** and by a very specialised **conductivity.**

STRUCTURE OF MUSCLE.

There are three forms of muscle in the human body: **non-striated muscle, striated muscle,** and **cardiac muscle.**

NON-STRIATED MUSCLE (syn. **plain, visceral, smooth**) consists of elongated or spindle-shaped nucleated cells, cemented together into membranes or bands by **intercellular substance,** which, like that of endothelium, can be demonstrated by staining with silver nitrate. They are pale in colour, and exhibit traces of longitudinal striation. The nucleus is generally elongated, and centrally placed.

Non-striated muscle forms a portion of the walls of all the hollow abdominal and pelvic viscera, of the lower half of the œsophagus, of the arteries, and of the veins and lymphatics, except the smallest; it occurs abundantly in the trachea and bronchi, in the iris and ciliary muscle, and in the skin it forms the muscles which cause the erection of the hairs. Its contractions are usually beyond the control of the will; hence it is sometimes called **involuntary muscle.** One non-striated muscle at least—the ciliary muscle of the eye—is an exception to this; its action is voluntary.

STRIATED MUSCLE is the most highly differentiated

contractile tissue. It forms the **skeletal muscles**—those attached to the bony skeleton—and also occurs in the pharynx and upper half of the œsophagus. It consists of **fibres** bound together into bundles—**fasciculi**—by fine connective tissue—**endomysium**—and these are again united by connective tissue of a coarser character—**perimysium**—to form 'a muscle,' as it is known to the anatomist.

Each striated muscle fibre is about 1 inch in length, and about $\frac{1}{500}$ of an inch in diameter, and consists of a tube—muscle tube, **sarcolemma**—formed of a delicate

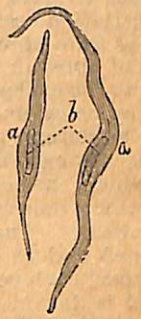


FIG. 5.—TWO MUSCLE CELLS FROM NON-STRIATED MUSCLE.

a, Cell substance; *b*, nuclei (×400).

elastic membrane, on the inner surface of which **nuclei** occur at intervals. The tube is filled with fluid muscle plasma—the **sarcoplasm**—in which a large number of **fibrils** are closely embedded. These fibrils run the whole length of the muscle fibre; each consists of dark and light portions arranged alternately, the summed effect of which confers upon the whole fibre a banded or cross-striated appearance.

The fibrils (not the sarcoplasm) are the actual contractile elements, for isolated fibrils from the muscle fibres of insects have been seen to contract when examined in white of egg. The light portion of each

fibril is divided across the middle by a dark line—**Dobie's line**: each dark portion is similarly divided by a light line—**Hensen's line.** The simplest unit, therefore, of muscle fibril consists of half a dark portion and the contiguous half of a light portion. During contraction the dark part swells, and the light part seems to disappear into the dark, being received, according to Schafer, into tubular pores in the latter.

The sarcoplasm possibly serves as a food-supply for the more active fibrils. The sarcolemma surrounding the whole fibre seems to have the property of insulating any (vital) excitation occurring in a given fibre, and of preventing it from spreading to other fibres. Thus a small group of fibres in a skeletal muscle may be made to contract to the exclusion of the other fibres. Cross-striated muscle, being under the control of the will, is often called **voluntary** muscle.

CARDIAC MUSCLE, though involuntary, possesses transverse striæ, which, however, are less marked than those of voluntary muscle. It forms the bulk of the wall of the heart. The fibres appear to be cylindrical cells joined end to end and uniting with each other by branches; each cell has an oval nucleus near the centre, and is devoid of sarcolemma. It is now generally believed that the cells of the heart form a **syncytium.** Further, it is a well-established fact that if any small portion of heart muscle is made to contract, the excitation as a rule does not remain limited to the portion first involved in contraction, but spreads thence over the whole heart. This fact receives a ready explanation on the syncytial view of heart-muscle structure.

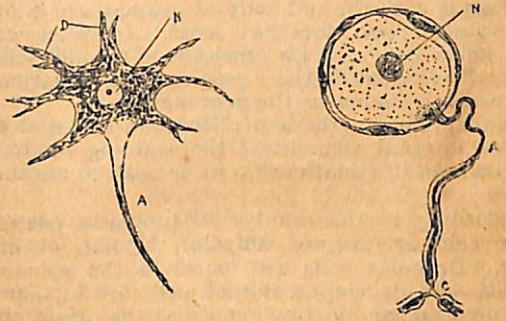
THE TISSUES OF THE NERVOUS SYSTEM.

These are either (1) **nerve cells** with their processes or (2) **neuroglia cells** and neuroglia fibres. The former are the active elements, the latter (confined to the interior of the brain and cord) supporting structures. Nerve cells occur both in the central nervous system (brain and cord) and in outlying ganglia; these latter

are of two kinds, autonomic and spinal-root, or sensory. Nerve fibres form most of the white matter of the brain and cord, and likewise form the essential part of the peripheral nerves; in the periphery they terminate in specialised **nerve-endings.**

NEUROGLIA consists of stellate cells with longish fibres which interlace to support the more important nerve elements.

NERVE CELLS vary exceedingly in shape, etc. Their



I. II.

FIG. 6.—NERVE CELLS.

I., Multipolar; II., Unipolar.
A., Axon; *D.*, dendrites; *N.*, nucleus; *C.*, constriction of Ranvier.

one constant character is the possession of an **axis-cylinder process** or **axon,** which becomes the axial part of a nerve fibre. All have a large round nucleus with distinct nucleolus. The cytoplasm of the cell body is usually continued outwards into long branching processes (**dendrites**), which are distinguished from the axon by their cytoplasmic structure. Thus they contain long-shaped or angular basiphil granules (**Nissl granules**), which are also brought out in the general nerve-cell protoplasm by staining with toluidin blue; whereas the axon—and the cone of origin of the axon—is free from granules.

In addition to the Nissl granules present in the cell body and dendrites, we can, by a special staining method (that of **Cajal**), recognise in them a meshwork of fine neuro-fibrils, which can also be traced outwards into the axon.

When nerve cells are stained by the **method of Golgi**, the cell bodies along with all the processes become intensely black and stand out very sharply. Two neighbouring cells are never seen to anastomose. The processes of one may come into close contiguity or **synapse** with the cell body or processes of another, but actual fusion does not occur. In other words, each nerve cell with its processes is an independent unit. This view of the 'geographical' relations of nerve cells is known as the **neurone theory.**

The staining methods of Nissl and of Cajal show special internal structures; the staining method of Golgi shows the relationship of one cell to another in space.

According to the number of processes possessed, nerve cells are termed **unipolar, bipolar,** or **multipolar.** Unipolar cells are found in the spinal-root ganglia. In development such cells are bipolar and become unipolar by convergence at the origin of two axon processes. In the sensory ganglia of the eighth cranial nerve the cells are bipolar. Most nerve cells are multipolar, with but one axon and many dendrites. The cells of the sympathetic ganglia are multipolar.

Nerve Fibres always originate from nerve cells. They are of two kinds, **medullated** (myelinate) and **non-medullated** (amyelinate). The former spring from the central nervous system; the latter from sympathetic ganglia, being known under a different connotation as **post-ganglionic** fibres. The non-medullated fibres consist merely of axon (with perhaps a delicate sheath) and are beset at intervals with nuclei. Each medullated fibre has a central axon enclosed in a thick fatty cylinder or **myelin sheath,** the latter being interrupted at intervals (**nodes of Ranvier**). In the nerve fibres of the peripheral nerves there is a thin outer enclosing sheath—the **neurolemma**—

which is beset with nuclei. Neurolemma and nuclei alike are absent in the nerve fibres that form the white matter of brain and cord.

NERVES AND NERVE TRUNKS.—An anatomical nerve is invested with a sheath of connective tissue, the **epineurium.** This conveys the blood and lymph vessels. In the nerve the fibres are gathered into separate bundles or **funiculi,** which are circular in section. Each funiculus is ensheathed in a special covering of connective tissue—the **perineurium**—which is arranged in a series of very thin **lamellæ** of white connective tissue covered with flattened endothelial cells. The intervals between these lamellæ are lymph-spaces, and drain lymph from the funiculi. Inside the perineurium the fibres are supported by a very delicate connective tissue, the **endoneurium.**

DEGENERATION AND REGENERATION OF NERVES.—If a nerve be cut, the fibres degenerate between the point of section and the point of distribution of the nerve fibres. The portions of the fibres which are in connexion with nerve cells remain intact, so that, besides the nourishment which the fibres obtain from the blood, there is a **trophic** influence exerted upon them by the nerve cells with which they are continuous, and from which they were originally formed.

The degeneration affects in the first instance the myelin sheath, which breaks up into droplets, and acquires a different staining reaction. The staining **method of Marchi** has been of great value in following these changes during the mapping out of the geography of the central nervous system. At a later stage the myelin sheath disappears. The staining method of **Weigert-Pal** has now to be employed. The degenerative changes occurring in the myelin sheath are known as **Wallerian degeneration.**

If conditions are suitable the divided axons in the central end grow peripherally, and tend to follow the distribution of the old neurolemma sheaths. This is only imperfectly accomplished, and full function never recurs. The rate of growth is about 1 inch per month. Where the neurolemma sheaths are absent, as in the central nervous system, regeneration never occurs.

NERVE ENDINGS.—Important terminations of efferent nerves are the **motor end-plates** in skeletal muscle, and the terminal arborisations found in involuntary and cardiac muscle and in secreting glands. Important efferent nerve endings are **tactile corpuscles, end-bulbs, corpuscles of Ruffini, corpuscles of Golgi, Pacinian corpuscles,** and **muscle spindles.**

CHAPTER V

THE NEURO-MUSCULAR MECHANISM

SKELETAL MUSCLE.

INDEPENDENT EXCITABILITY.—If the nerve to a cross-striated muscle be cut, complete inactivity or paralysis of the muscle ensues. From this it is deduced (1) that the muscle is normally thrown into action by a 'message' transmitted along the nerve; (2) that the muscle of itself has **no power of automatic action.** Nevertheless, if a stimulus (electrical, mechanical, chemical, or thermal) is directly applied to a muscle whose nerve has been cut, the muscle contracts. In other words, the muscle possesses **irritability** or **excitability;** it can be excited to action by a stimulus.

But a muscle is permeated with nerves and nerve branches. Can one be sure that the muscle itself has **independent excitability** apart from the nerve? Two proofs of the independent excitability of muscle may be given: (1) The sartorius muscle of the frog is devoid of nerves at each end; a stimulus applied to either end causes contraction. (2) Curare paralyses the junction of nerves with muscles, the so-called myoneural junctions; consequently stimulation of the motor nerves of a curarised animal causes no muscular contraction; yet these muscles respond to direct stimulation when they have been denervated, as it were, by the drug.

THE MUSCLE TWITCH.—When effective stimuli are applied to a muscle, the result may be of two kinds, according to the nature of the stimuli. Either there

occurs a contraction followed immediately by relaxation (known as a **simple twitch**) or there is a sustained contraction. The contractions are studied by the graphic method. A simple twitch shows (1) a **latent period,** lasting about $\frac{1}{100}$ second; (2) a **phase of contraction,** lasting say $\frac{4}{100}$ second; and (3) a **phase of relaxation,** whose duration is about $\frac{5}{100}$ second, the total time for the whole series of events, in the case of a fresh frog-muscle, being about $\frac{1}{10}$ second. All responses of muscle elicited by one single stimulus are of this short jerky nature.

TETANIC CONTRACTIONS.—When a muscle after twitching once is excited by a second stimulus, it twitches a second time, and so on. If, however, the second stimulus is timed to arrive during the first contraction, the muscle contracts to a greater height than before, the second twitch being as it were **superposed** on the first; and the total time of contraction is greater. Similarly, if the muscle is excited by a series of stimuli in rapid succession, it responds by a prolonged contraction, which may be quite uniform if the rate of stimulation is sufficiently great (more than 30 per second). To obtain a sustained contraction, it is necessary that the muscle be subjected to **a rapid series of stimulations.** This is what occurs when a muscle is contracted voluntarily.

THE MUSCLE WAVE.—When a muscle contracts, it undergoes **no change of volume.** The loss in length is exactly counterbalanced by an increase in thickness. Further, contraction always begins in the portion first stimulated, and spreads thence to distant parts—in other words, there is a mechanism for **conductivity** in the muscle. The rate of spread may be measured by allowing two levers to rest on the side of a curarised muscle, one at each end, the muscle being excited at one end. The fact that the trace of each lever resembles a simple twitch shows that a **wave of contraction** passes along the muscle. This wave, which is transmitted equally well in either direction, travels at a rate of 3 metres per second.

HEIGHT OF CONTRACTION A FUNCTION OF STIMULUS.—If we vary the strength of the stimulus applied,

the height of the muscle contraction also varies. A very weak stimulus may elicit no response. A stronger stimulus may just elicit a feeble response. With further increase in the strength of the stimulus, the height of contraction increases up to a certain point (**maximal contraction**), after which no further increase takes place, although the stimulus may continue to go on increasing. The smallest contraction is called a **minimal contraction**; the stimulus that arouses it is also called **minimal.** Contractions less than maximal are called **submaximal.**

THE MUSCLE FIBRE ALWAYS CONTRACTS MAXIMALLY. —Although the height of contraction of the muscle *as*

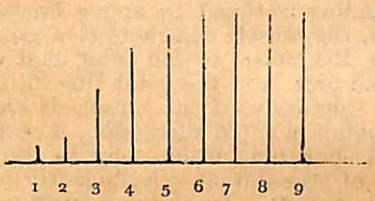


FIG. 7.—DIAGRAM SHOWING INCREASE OF MUSCLE CONTRACTION DUE TO INCREASE OF STIMULUS.

1, Minimal; 2-5, submaximal; 6-9, maximal contractions.

a whole can be graded, the individual fibres of which it is composed, when they do contract, invariably contract to the full. If a uniformly weighted muscle, consisting of a very few fibres, is stimulated with gradually increasing stimuli, the rise in height of the contraction takes place not continuously, but by a series of well-marked steps, indicating that each new increment in the height of contraction is due to the participation of fresh groups of muscle fibres. The fibres in a muscle form a group of **isolated units.** The height of contraction in a simple twitch depends upon the *number* of fibres involved.

EXTENSIBILITY AND ELASTICITY.—Muscle is extensible and elastic. When resting muscle is extended by successive equal increments of weight, the succes-

sive increments of extension become less and less—*i.e.*, Hooke's Law is not obeyed. Contracting muscle is relatively more extensible than non-contracting muscle. After extension, the muscle more or less regains its previous length—*i.e.*, it has a high degree of **elasticity.**

WORK OF MUSCLE.—Physical work is measured by the product of force into the distance through which the force is exerted (work=$f \times d$; or in the case of a weight w, lifted through a height h, work=$w \times h$). Thus it is easy, knowing the height through which a given weight is lifted by a muscle, to calculate the work done. A muscle may be thrown into activity, and yet perform no external work. This happens when it is prevented from shortening. The muscle, as it were, tries to contract, but it is unable to bring the two points of attachment closer together; it *develops tension* which, however, is unable to overcome the counterforces. Such activity of a muscle is called **isometric contraction** as opposed to **isotonic contraction,** in which the muscle moves, but the weight, and therefore the tension, remains the same. Although the muscle performs no external work in isometric contraction, energy is used up in producing the state of tension.

CHEMISTRY OF MUSCLE CONTRACTION.—Muscle in order to produce work can utilise carbohydrates, proteins and fats, but it is mainly from carbohydrates that it derives its energy. The actual factor, however, which produces the contraction of muscle when stimulated *is not yet known.* The chemical composition of muscle is fairly well defined, but the chemical changes which accompany the contraction of muscle are still the subject of investigation. Resting muscle is composed mainly of the following constituents: water, 80 per cent.; protein, 18 per cent.; glycogen, 0·7 per cent.; phosphagen, 0·5 per cent.; adenylic acid pyrophosphate, 0·3 per cent.; carnosine, 0·3 per cent.; lactic acid, trace. **Phosphagen** is a combination of creatine with phosphoric acid.

It has been suggested that during stimulation glycogen and phosphagen are hydrolysed respectively into lactic acid and into creatine plus phosphoric

acid. These reactions are *exothermic—i.e.*, they give out heat, and they occur whether oxygen is or is not present. During relaxation, if sufficient oxygen is present, the lactic acid and the creatine plus phosphoric acid are resynthetised into glycogen and phosphagen respectively. The energy required for this is obtained from the oxidation of part of the lactic acid to CO_2 and H_2O. In the *absence* of oxygen the only energy available for the resynthesis of the phosphagen is the exothermic hydrolysis of glycogen into lactic acid. This energy is very small, and the muscle very shortly ceases to function. Phosphagen disappears and lactic acid accumulates.

In support of this hypothesis is the observation that sodium iodoacetate prevents the formation of lactic acid from glycogen, but does not prevent the hydrolysis of phosphagen, and if a muscle has been poisoned by this substance, then the resynthesis of phosphagen cannot occur. The muscle ceases to contract after performing about one-third the normal amount of work. The phosphagen disappears, but no lactic acid appears.

Although the chemical changes just outlined form a convenient basis upon which to study the chemistry of muscle contraction, it does not take into account the intermediary processes which occur. This hypothesis, moreover, implies that the energy necessary for the resynthesis of phosphagen is derived from the combustion of carbohydrates, but there is evidence to suggest that other sources may be available. Although no finality has yet been reached, there is shown on page 33 a schematic representation of what has been suggested as a likely occurrence.

In the living animal any excess lactic acid will combine with the $NaHCO_3$ present to form sodium lactate. On reaching the liver, the lactate radical will be converted into glycogen, and this will be liberated eventually in the form of glucose. When this glucose reaches the muscles, it will again be stored as glycogen.

THERMAL CHANGES.—On stimulating a nerve-muscle preparation, the hydrolysis of the glycogen, and

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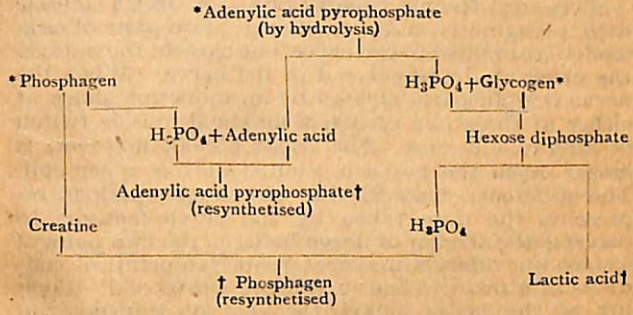
phosphagen gives rise to heat. This heat is evolved whether or not oxygen is present, and is known as **initial heat.** If no oxygen is available, the lactic acid will remain in the muscle. If, however, oxygen is present, then after relaxation part of the lactic acid will be reconverted into glycogen. The energy to do this is obtained from the oxidation of the remainder of the lactic acid to CO_2 and H_2O, as already stated. Heat is evolved in the process and is known as **recovery heat.** This, although more prolonged in its production than the initial heat, is practically equal to it in amount.

When muscles *in situ* are subjected to excessive



activity, as in running or climbing, then it may happen that the products of activity (*e.g.*, lactic acid) are produced more rapidly than can be dealt with by the available oxygen supply in the blood. These by-products are oxidised during the subsequent recovery, and the extra oxygen utilised in this period, as compared with the oxygen consumption of the normal resting individual, is a measure of the **oxygen debt.**

These observations on the chemical changes occurring during muscular contraction apply to skeletal muscle. The factors causing contraction in cardiac and visceral muscle are not yet fully understood.

* Present in muscle before contraction.
† Present in muscle after contraction.

Nerve.

The change in a muscle during activity can be seen and felt; activity in a nerve is invisible and impalpable; nerve is entirely *devoid of contractility*. It possesses, however, **excitability**—*i.e.*, a stimulus applied to any portion along its length can excite a vital process in the portion immediately stimulated. It also possesses **conductivity**—*i.e.*, the vital process once started in any short length of the nerve itself affects immediately adjoining portions, which in turn affect others, and so on. The property of conductivity is the essential function of a nerve.

Rate of Nerve Conduction.—A frog's muscle with a long nerve is dissected out. Two pairs of electrodes are applied to the nerve, one close to the muscle, the other at the upper end of the nerve. When the nerve is sufficiently excited by an induction shock at either of these two places, a maximal muscle twitch in each case occurs. The latent period, however, is longer when the nerve is excited at the upper end. The difference between the two latent periods represents the time taken by the nerve message to traverse the stretch of nerve between the two pairs of electrodes. Frog's nerve at room temperature conducts at a rate of about 20 metres per second. Cooling of the nerve delays the rate of transmission. Human nerve, which is permanently maintained at a constant and fairly high temperature, conducts at a rate of 120 metres per second.

Electrical Change accompanying Nerve Activity.—Though the existence of nerve activity is under ordinary conditions only *inferred* from the fact that an end-organ, such as a muscle, responds when the nerve is stimulated, nevertheless there are means of detecting directly whether a nerve is active or not. If a nerve is excited, say, by pinching, the portion pinched immediately changes its **electrical potential** and becomes **negative** to any other part of the nerve. This change of potential is entirely transient; next moment it is found that an adjoining part of the nerve has become negatively charged, whereas the portion

first stimulated returns to its previous (neutral) potential. Indeed, the change of potential sweeps along the nerve at precisely the same rate as the ordinary message is transmitted, being likewise accelerated by warming of the nerve and delayed by cooling. Whenever the nerve transmits a message, this electrical change accompanies the message, so much so that some physiologists have claimed that the transmitted electrical change *is* the message.

THE NERVE IMPULSE.—The electrical change is transmitted in the form of a **wave.** Considering any short length of a nerve through which a message is being conducted, it is found that the potential of this short portion rapidly acquires maximum negativity and then uniformly returns to the previous neutral condition. The whole change is of course enormously rapid, but its wave-like nature is unmistakable. Evidently in activity some **upset of molecular equilibrium** occurs which is followed by a **return** to the previous state. This transmitted double process—viz., upset of equilibrium and return to the *status quo ante*—is called a **nerve impulse.** It is transmitted equally well in either direction.

When a long parallel-fibred *muscle* is excited at one end, a precisely similar **wave of negative potential** starts at the portion first excited, and sweeps along to the other end. The duration of this wave, or **muscle impulse,** is very short and just precedes the contraction wave. It is considered to represent the conducted process in the muscle, which awakens each successive part subsequently to contract. The electrical change, both in nerve and in muscle, is intimately related therefore to conductivity.

REFRACTORY PHASE.—When any short length of a nerve is for the moment engaged in the transmission of an impulse, it is during that time inexcitable to further stimuli. In other words, it has a **refractory phase.** This period of inexcitability, due to its being already engaged in activity, is under ordinary circumstances short, not much more than $\frac{1}{1000}$ second. At the end of this interval it is ready to conduct another impulse. It is found also that by shortening the interval

sufficiently between two stimuli it is impossible to superpose one electrical change upon another. A second electrical change does not occur, if at all, until the first is almost completely over. The refractory phase is therefore closely associated with the duration of the electrical change. Such experiments teach that a nerve is capable only of **intermittent** activity, each transmitted impulse being distinct from the others. The activity of a nerve excited by stimuli in rapid succession is like a flicker, and never like a continuous glow. Furthermore, the activity of each fibre is probably of an **all or nothing** nature.

Afferent and Efferent Nerves.—The nerve fibres present in the posterior spinal nerve roots convey impulses towards the cord: these are called **afferent** or **sensory** fibres. All the fibres in the anterior roots convey impulses outwards to muscles, glands, etc. These fibres are **efferent.** Although a nerve fibre is structurally capable of transmitting impulses in both directions, one and the same nerve fibre is never in the normal economy used for such double transmission.

Qualitative Differences in Nerve Messages.—The individual impulses that travel along afferent and efferent fibres are probably all alike. The messages may conceivably differ, however, in the interval between the individual impulses—*i.e.*, there may be a difference in the rhythm of pitch of a (more or less) rhythmical series.

Agents and Influences that depress Conductivity.—Long-continued **withholding of oxygen** from a nerve; **anæsthesia** by means of ether, chloroform, etc.; **exposure to carbon dioxide vapour, mechanical compression, cooling**; and the presence of a **positive pole** of an electric current—all tend to abolish conductivity, which, however, may in every case return on removal of the depressing agent.

Motor Nerve Cells.—The nerve cells that send impulses to the skeletal muscles are of the multipolar type. The spinal motor nerve cells lie in the anterior horn of the grey matter. Such motor nerve cells are not capable of spontaneous action. They are thrown

into activity either by impulses from the afferent nerves passing into the cord or the brain (**reflex action**), or by voluntary impulses arising in the cerebral cortex (**voluntary muscular movement**).

FATIGUE OF THE NEURO-MUSCULAR MECHANISM.—If a nerve-muscle preparation is repeatedly stimulated the individual muscle-twitches gradually become cut down in extent, while contraction and especially relaxation are greatly slowed. Eventually the muscle ceases to respond to stimulation of the nerve. The seat of the complete fatigue lies therefore either in the **muscle,** in the **myo-neural junction,** or in the **nerve.**

The muscle will still respond to direct stimulation when it has ceased to respond to stimulation of its nerve. Therefore the muscle does not give way first. By testing the electrical reactions of the nerve, it can be shown that it is not fatigued. Hence the first fatigue is in the myo-neural junction.

Voluntary muscle fatigue in the living subject, which involves function of the nerve cells, is studied with the ergograph. When an individual, by voluntary effort, can no longer use his muscles, stimulation of the nerves by electrodes applied over the skin produces good muscular contraction. Hence the central nerve cells first give way. The relative **order of fatigability** is as follows:

1. Nerve cells.
2. Myo-neural junctions.
3. Muscle.
4. Nerve, which can be fatigued only with the greatest difficulty.

REFLEX ACTION.—Examples of reflex action are such movements as occur for example in coughing, in sneezing, and in the withdrawal of a limb in response to an irritant. They are never voluntary movements, but occur as it were automatically. We can trace the source of each to a sensory stimulus.

A **reflex arc,** consisting of a sensory neurone with its special termination (the **receptor organ**) and of a motor neurone with attached muscles (the **effector**

organ), forms the anatomical basis for an ordinary reflex. The stimulus is conducted first *to* the central nervous system by the sensory nerve, and then *from* the central nervous system to the muscle in question. The efferent conductor may be a secretory nerve going to a gland (*e.g.*, parotid). Damage to *any* part of the reflex arc destroys the reflex.

THE SPINAL ANIMAL.—Though many reflexes are mediated by parts of the brain, they are best studied in an animal (preferably cold-blooded) whose brain

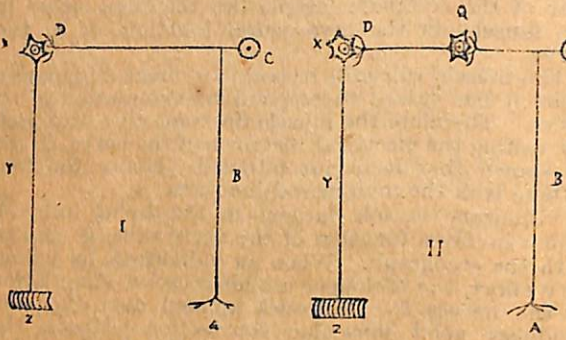


FIG. 8.—DIAGRAM OF REFLEX ARC.

I., Simpler form; II., more complex form.

A, Receptor organ; *B*, afferent nerve fibre, with *C* its nutrient cell; *D*, synapses; *X*, motor nerve cell; *Y*, efferent nerve fibre; *Z*, effector organ (muscle); *Q*, intermediate neurone.

has been destroyed. Immediately after the operation the reflexes are in abeyance—**shock.** The cord, however, gradually recovers its irritability. The animal makes no *spontaneous* movement, but on being stimulated makes responses that closely simulate voluntary movements, though carried out unconsciously. If the foot is pinched (**pathic stimulus**) the leg is withdrawn (**flexion response**); if the sole of the foot is pressed, the toes are spread as in walking, and so on. Purposive movements of this nature are **co-ordinated**

reflexes. Other examples are the scratch reflex in a spinal dog, walking reflex, clasp reflex in a male frog, micturition, defæcation, ejaculation, parturition, and tendon reflexes, such as the **knee-jerk.**

THE RECEPTOR ORGAN.—Co-ordinated movements are obtained only on stimulation of the normal sensory terminals, never on stimulation of an exposed nerve, in which latter case the result is a disorderly movement, or **inco-ordinated reflex.** Each group of sensory terminals is pictured as being linked up with a special group of motor neurones. Again, in the same area of skin there may be more than one kind of sensory end-organ, and according to the form of stimulation so is the response: thus pricking the sole causes flexion of the limb; generalised even pressure applied to the sole causes extension. Each end-organ, besides being linked up with its own motor neurones, is attuned to its own special form of stimulation.

THE CONDUCTING MECHANISM, which includes synapses, differs from mere conduction along a nerve. (1) The **speed** is slower, for delay occurs at the nerve-synapses. The more neurones that are intercalated between the fundamental sensory and motor neurones, the greater is this delay. The time that elapses between stimulation and response is the *reflex time.* (2) Conduction in the reflex arc is readily **inhibited** by activity in other parts of the central nervous system. The cerebrum exercises an inhibitory action on reflexes occurring in the cord. (3) Conduction occurs only in one direction—**law of forward direction.** (4) **Strychnine** greatly modifies conduction in the reflex arc, increasing excitability and changing co-ordinated into inco-ordinated reflexes. (5) Reflex arcs are subject to **fatigue,** the fatigue occurring at the synapses.

AXON REFLEXES.—In connection with the function of *plain muscle tissue—e.g.,* of the bladder and bloodvessels—a peculiarly simple form of reflex is found, which involves no synapses, and in which the 'reflexion' takes place at the axon-branching of one and the same nerve fibre (for an example see p. 70). Such reflexes, which do not involve conduction through the central nervous system, are termed *axon reflexes.*

CHRONAXIE.—An excitable tissue, such as muscle or nerve, may be stimulated by various means—thermal, chemical, mechanical, electrical. For purposes of comparison between different tissues, the electrical method is usually chosen, being easiest to control and least damaging. It has been found that there are two factors in an electrical stimulus which determine its efficiency—(*a*) the *strength* of the stimulus, (*b*) the *duration* of its application. The figure representing the latter is known as the chronaxie (lit. 'time value'), and is found as follows: A galvanic current of 'unlimited' duration—that is, about ·01 second or longer—is applied to the tissue. The *strength* is gradually diminished until, on the application of such a stimulus, only a faintly perceptible movement of the muscle is seen. The strength of this stimulus is found by means of a voltmeter. This is called the **rheobase.** The current is now increased in strength to *twice* the rheobase. and this reinforced current is applied to the tissue for exceedingly short intervals of time. The shortest period of time that will just give a faintly perceptible twitch of the muscle is called the chronaxie. For the gastrocnemius of the frog it has a value of about ·0003 second.

It has been shown that groups of muscle which ordinarily work in conjunction have the same chronaxie for each muscle in the group.

MUSCLE TONUS.—By reflex action a slight contraction of skeletal muscles, especially those concerned in the maintenance of posture, is permanently maintained, owing to afferent stimuli streaming into the cord from **muscle spindles** and **organs of Golgi.** Destruction of the central nervous system or of either the motor *or* the sensory nerve roots abolishes this **tone.** It is also abolished by deep general anæsthesia, as is employed in reducing dislocations of limbs.

RECIPROCAL INNERVATION.—When flexion of a joint occurs by reflex action, a simultaneous inhibition of tone of the antagonistic muscles occurs, and *vice versa.* This combined effect is known as **reciprocal innervation.**

THE NATURE OF VOLUNTARY MUSCULAR CONTRACTION.—Voluntary muscular contraction is tetanic. By electrical investigation it has been found that the stimuli descend the motor nerves at a rate of 50 to 70 impulses per second, being discharged as 'volleys' and not at irregular intervals, by the corresponding groups of motor nerve cells. Reciprocal innervation involving abolition of tone in antagonistic muscles also occurs.

CHAPTER VI

THE BLOOD

THE blood consists of a viscid, straw-coloured fluid, called **plasma,** or **liquor sanguinis,** in which a vast number of minute yellowish solid discs—**red blood corpuscles**—a smaller number of protoplasmic cells—**colourless (white) corpuscles**—and many minute flattened bodies—**blood platelets**—are suspended.

Its specific gravity is 1·058.

Although the blood is entirely contained in the heart and bloodvessels—the arteries, capillaries, and veins—there exudes through the walls of the capillaries a fluid called **lymph,** which is similar in composition to plasma, but contains less protein. This acts as an intermediary between the blood and the tissues, conveying nourishment to them, and carrying away waste products. The lymph leaves the tissues by means of lymphatic vessels, and is eventually returned to the blood by the large lymphatic ducts, which empty their contents into the subclavian veins. The colourless corpuscles may also pass through the walls of the capillaries. This is known as **diapedesis.**

The spleen presents an exceptional condition, as the capillaries of this organ terminate in tissue spaces, or lacunæ; so that the blood, instead of passing directly from the arterial to the venous capillaries, passes through the spongy tissue of the spleen. This, along with the placenta, the medulla of the suprarenal glands, and the liver, are the only organs in the higher animals in which there is any discontinuity in the walls of the bloodvessels.

THE FUNCTIONS OF THE BLOOD are—

1. To convey **oxygen** to all the tissues and organs of the body.
2. To remove carbonic acid and other **waste products** from the tissues and organs, so that they may be excreted through the medium of the lungs, skin, and kidneys.

3. To distribute **nourishment** to all the tissues.
4. To distribute the so-called **internal secretions** which are formed in such organs as the thyroid, suprarenals, etc.
5. To distribute heat and **regulate temperature.**

Blood Plasma, or Liquor Sanguinis.

The **plasma** of the blood is a viscid fluid with a specific gravity of 1·028. It contains three proteins in solution, **fibrinogen, serum globulin** and **serum albumin,** together with extractives, fat and inorganic salts. The principal salts are—sodium chloride, calcium phosphate, sodium bicarbonate and potassium sulphate.

Plasma may be obtained by **cooling** the shed blood to less than 5° C., or by adding large quantities of **neutral salts,** or by adding **oxalates.** In each case the corpuscles are allowed to sediment, and the plasma can be drawn off. If the above precautions are not taken the blood will **coagulate.**

The Coagulation of the Blood.—When blood is withdrawn from the bloodvessels of the living body, it sets and forms a tremulous solid mass in from three to ten minutes. This is due to the formation of **fibrin,** which solidifies the whole. The fibrin gradually contracts, enmeshes the corpuscles and squeezes out the **serum** from the clot. The process is completed in from twenty-four to thirty-six hours. The clot then sinks in the straw-coloured serum.

The formation of the clot is accelerated by anything which hastens the disintegration of the platelets. On the other hand, all agencies that delay or prevent disintegration of the platelets delay or prevent coagulation of the blood.

Coagulation occurs **more rapidly** when blood is (1) agitated, (2) kept at body temperature, (3) in contact with a foreign body.

Coagulation occurs **less rapidly,** or not at all, when blood is (1) at rest and surrounded by oil; (2) cooled; (3) in contact with healthy living vessel-wall; (4) mixed with an oxalate, thereby causing the soluble calcium

salts to be precipitated as insoluble calcium oxalate; (5) mixed with a soluble citrate, which reduces the ionisation of the calcium; (6) mixed with a neutral salt in large quantities; (7) mixed with leech extract. Coagulation is also prevented when peptone has been injected into the bloodvessels.

The origin of the fibrin has given rise to much controversy, but it is believed that the following is a satisfactory explanation. Platelets and connective tissue cells when damaged liberate a ferment called **thrombokinase**; this *in the presence of ionised calcium salts* reacts with **prothrombin** (in the plasma) to form **thrombin.** The thrombin now reacts with the soluble fibrinogen and forms insoluble **fibrin.**

In order to explain the absence of intravascular clotting due to the accidental formation of thrombin in the circulating blood, it is suggested that small amounts of **anti-thrombin** are present in the plasma. Such a substance is found in the head of the leech and is known as **hirudin.** A preparation called **heparin** has been extracted from liver tissue, and this substance has been found to neutralise *prothrombin.*

Serum, as already stated, is the fluid which separates from the clot. It differs from plasma in containing no fibrinogen. There may be present, however, traces of thrombokinase and thrombin. Serum reacts **alkaline** to **litmus.** This can be demonstrated by touching glazed litmus-paper with blood, and washing it off immediately with a stream of distilled water. The blood contains a small excess of hydroxyl over hydrogen-ions, and has a pH of 7·34 at body temperature.

The Blood Corpuscles.

The coloured or **red blood corpuscles** (**erythrocytes**) are minute biconcave discs averaging 7·3 μ (microns) in diameter, and about 2·5 μ in thickness. They have a higher specific gravity than the liquor sanguinis—1·088, whilst the latter is 1·028; so that they tend to sink in it: this sinking is accelerated by their adhesion in **rouleaux,** like piles of coins.

Number.—In the healthy male adult there are about 5,000,000 corpuscles in every cubic millimetre of blood; in the female 4,500,000. These bodies render the blood **opaque** even in extremely thin layers.

Structure.—When blood is diluted with water, the blood corpuscles first become bell-shaped, then spherical, and then lose their colour, as the colouring matter —**hæmoglobin**—escapes into the diluted plasma. Blood so treated is transparent, and has the appearance of a solution of carmine; hence it has been called **laked blood.** Distilled water lakes the blood corpuscles as a result of **osmotic swelling.** Ether and chloroform, bile salts, saponin, snake-venom and alkalies lake the blood by dissolving the envelope.

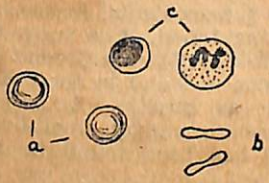


FIG. 9.

a, Coloured blood corpuscles; *b*, the same seen edgewise; *c*, colourless corpuscles.

Furthermore, blood may be laked by the action of foreign sera. Any substance that discharges hæmoglobin from the red blood corpuscles is known as a hæmolytic agent, and the process of laking is often termed **hæmolysis.**

In some animals, as the frog, the blood discs are nucleated. In man and other mammals the red blood corpuscles are non-nucleated, and the cell is structureless as far as we are able to examine it; many people believe that it consists simply of a hollow **envelope** containing hæmoglobin. The corpuscle is elastic, so that the cells alter their form on compression.

Concentrated saline solutions cause the blood corpuscles to become **crenated,** or toothed round their margin. This again is the result of osmotic action.

HÆMOGLOBIN is a complex body, known as a 'conjugated protein,' consisting of an elementary protein —**globin**—united with an iron-containing pigment—**hæmatin.** In the case of human blood, the hæmoglobin decomposes very rapidly, and becomes converted into globin and hæmatin: if hæmoglobin is kept at a freezing temperature, and in an atmosphere free from oxygen, this does not happen, but the **hæmoglobin crystallises** in prismatic plates.

The relations of hæmoglobin to oxygen are very important, as this substance forms the medium by which oxygen is carried from the lungs to all parts of the body. In the lungs hæmoglobin absorbs oxygen, which enters into a loose chemical union with it. Hence, hæmoglobin exists in two conditions: **oxyhæmoglobin,** and deoxidised or **reduced hæmoglobin.** Deoxidation occurs in the tissues.

The colour of the blood depends on that of the corpuscles; it varies according to the vessel from which it is taken. That from an artery is bright scarlet, that from a vein is dark maroon; hence bright blood is called **arterial,** and dark blood is called **venous.**

The changes of colour in the blood are entirely due to the oxidation and reduction of the hæmoglobin.

An **analysis** of coloured blood corpuscles shows them to consist of—

Water	63
Solids	37
	100

The solids in 100 parts are, approximately:

Hæmoglobin	95
Other proteins, Lecithin, Cholesterol, Ash	5

The ash yields a comparatively large quantity of **potassium salts.**

HÆMOGLOBIN COMPOUNDS.—**Oxyhæmoglobin** is a loose chemical combination of oxygen with hæmo-

globin. The oxygen can be removed (*a*) by subjecting the compound to a **reduced pressure** in an air-pump, in which case the O comes off suddenly, and not gradually as the pressure is reduced—in this process each gramme of oxyhæmoglobin gives off 1·34 c.c. of oxygen; or (*b*) by adding some fresh **ammonium sulphide** or a few drops of Stokes' reagent. Oxyhæmoglobin presents in the spectroscope a **spectrum** with two **absorption bands** between the D and E lines —*i.e.*, in the yellow-green portion.

Methæmoglobin is a more stable combination of oxygen and hæmoglobin, and differs from oxyhæmoglobin. It is formed when concentrated potassium ferricyanide or amyl nitrite is added to diluted blood. It is found in the urine when there is a breaking down of the red corpuscles and a setting free of hæmoglobin. It presents, besides the two typical bands of oxyhæmoglobin, a characteristic band between the C and D lines—*i.e.*, in the red. Reducing agents, such as fresh ammonium sulphide, convert methæmoglobin into hæmoglobin. It cannot, however, be reduced simply by exposure to a vacuum, and thus is **useless for respiratory purposes.**

Carboxyhæmoglobin, due to the combination of carbon *monoxide* with hæmoglobin, is formed (*a*) when coal-gas is passed through blood, or (*b*) when the fumes from the incomplete burning of carbon (as in charcoal stoves) are taken into the lungs. Its spectrum is very like that of oxyhæmoglobin, but it is not reducible by ammonium sulphide or Stokes' reagent. It gives to the blood a very bright scarlet colour, and prevents the union of oxygen with hæmoglobin.

Hæmatin is a brownish-red granular derivative of hæmoglobin, which forms crystalline compounds with the halogens known as **hæmins,** the chlorine compound of which, obtained by heating some blood on a slide with glacial acetic acid and sodium chloride, is also known as **Teichmann's crystals.**

Polycythæmia is an increase in the red corpuscles per unit volume of blood and may occur wherever there is an excessive loss o water—*e.g.*, complete starvation (concentration polycythæmia), or when the

person is exposed to low atmospheric pressures, as at high altitudes (compensatory polycythæmia).

Reticulocytes.—These are immature erythrocytes exhibiting a finely reticular appearance when treated with 'vital' stains. They form less than 1 per cent. of the circulating red blood corpuscles. After severe hæmorrhage their proportion may rise to over 30 per cent.

WHITE BLOOD CORPUSCLES, OR LEUCOCYTES.—These colourless blood corpuscles are nucleated pro-

FIG. 10.—COLOURLESS BLOOD CORPUSCLES, SHOWING THE VARIOUS FORMS ASSUMED BY A SINGLE CORPUSCLE WHILST UNDER OBSERVATION.

toplasmic cells. The nuclei are readily demonstrated under microscopical observations by the addition of **very dilute acetic acid** to the blood. Many of the colourless corpuscles exhibit active **amœboid movements.**

When white blood corpuscles are examined without the addition of staining reagents, they are seen to be of at least two varieties, **hyaline** (lymphocytes) and **granular** (leucocytes proper). Chiefly with the help of staining reagents these can be differentiated into five classes:

1. Small lymphocytes } hyaline.
2. Large lymphocytes }

3. Polymorphonuclears (neutrophils)
4. Eosinophils
5. Basophils

} granular.

The hyaline forms are believed to take their origin in **lymphoid tissue** (lymph glands, tonsils, Peyer's patches, etc.); the granular forms are derived from **red bone marrow.** The polymorphonuclear leucocytes, forming about 70 per cent. of the total leucocytes, are the chief phagocytes of the blood. The lymphocytes, which form nearly 30 per cent., are greatly increased in the blood after a meal, and diminish in number after fasting. The average number of white blood corpuscles per cubic millimetre is 5,000 to 7,000.

Leucocytosis is an increase in the number of colourless blood corpuscles. It may occur physiologically during digestion, after muscular exercise, and in pregnant women. When a diminution in the number of leucocytes takes place (as in certain pathological conditions—*e.g.*, typhoid fever) the condition is known as leucopenia.

Blood Platelets (Thrombocytes).—These are very small bodies found in blood in varying numbers. They are colourless and irregular in form, and in diameter are about one-fourth of a coloured corpuscle. In shed blood they rapidly adhere to form clumps of varying size. They likewise adhere to any part of the interior of a bloodvessel from which the endothelium has become denuded, forming a so-called **white thrombus.** They help to arrest hæmorrhage from a cut vessel by sticking in masses to the cut edge. Long regarded as artificial precipitates from the blood plasma, they are now known to be nucleated cells, and show irreversible flowing movements on extravasation. It is from them that thrombokinase is derived.

History of the Coloured and Colourless Corpuscles.—The coloured blood corpuscles are continually being broken up and renewed during life. The close relation of the bile pigment to hæmoglobin indicates that the bile pigment comes from the colouring matter of degenerated coloured corpuscles,

and it appears that the destruction of coloured corpuscles takes place for the most part in the circulating plasma.

The **development** of the coloured corpuscles, which has been largely studied in the developing chick, takes place as follows: At a very early stage a part of the embryo is surrounded by a **vascular area** consisting of branched mesoblastic cells. These become hollow, and their branches unite with branches of neighbouring cells to form primitive vessels. These cells appear

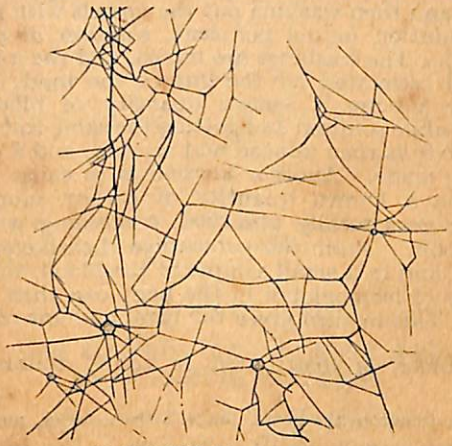


FIG. 11.—FIBRIN IN PROCESS OF FORMATION IN THE PLASMA.

to undergo rapid division towards the spaces within them, and thus a number of small nucleated cells (normoblasts), which become coloured discs, are formed. These undergo rapid division, and when the liver, spleen, and thymus are developing, many similar coloured discs become formed within their substance. Such nucleated coloured discs may develop directly into the mature non-nucleated coloured corpuscles, but the latter are mostly formed separately in the **red marrow**, which is the only manufactory in the adult. As was already stated, the

granular leucocytes likewise originate in the red marrow, which contains a vast number of polymorphs and especially of coarsely granular eosinophils and basophils. For factors affecting the development of the red blood corpuscles and their relation to the anæmias see Appendix.

Quantity and Distribution of the Blood.—About one-fifteenth of the weight of the body consists of blood. This has been estimated in animals by allowing as much blood as possible to escape from the vessels, and then washing out the vessels with **normal saline** solution (a 0·9 per cent. solution of sodium chloride). The washings are mixed, and the quantity of blood estimated by the tint of the fluid; this is done by mixing a known quantity of blood and normal saline solution and getting the same tint. The whole body is then minced and washed, and a similar estimate made. Another method is to cause a man to inhale a known quantity of carbon monoxide. This becomes totally absorbed, combining with the hæmoglobin. From the percentage of carboxyhæmoglobin found in a small sample of the blood, the total quantity of hæmoglobin in the body can then be deduced. This in turn gives the total amount of blood present.

The blood is distributed in round numbers as follows:

About one-fourth in the heart, lungs, large arteries, and veins.
" " liver.
" " skeletal muscles.
" " in other organs.

Blood Groups.

In the red blood corpuscles of some human beings are substances called **agglutinogens.** These corpuscles will clump together, i.e. *agglutinate*, if mixed with plasma containing their specific **agglutinins.** There are two agglutinogens, A and B, and *four* possible variations of these occur, A + B, A, B, and *no* agglutinogens, constituting the so-called groups.' The specific agglutinins are designated α and β. No one blood can contain *both*, an agglutinogen and its agglutinin. This becomes of importance in blood transfusion, when care must be

taken not to transfer a blood containing, say, A to a recipient whose blood contains *a*. Some bloods (group 1) contain no agglutinins, therefore these are 'universal recipients'; other bloods (group 4) contain no agglutinogens and are therefore 'universal donors.' This can be conveniently shown in tabular arrangement:

		Recipient's Blood.			
	Groups.	1.	2.	3.	4.
		o	*β*	*a*	*a*+*β*
Donor's Blood.	1. A+B	+	o	o	o
	2. A	+	+	o	o
	3. B	+	o	+	o
	4. O	+	+	+	+

In the above table the sign + indicates that the bloods are compatible with each other.

CHAPTER VII

THE HEART—CIRCULATORY AND LYMPHATIC SYSTEMS

The Heart and Bloodvessels.

The Heart.—The **heart** is a hollow muscular organ; its function is to propel the blood through the bloodvessels. It is enclosed in a **serous sac**—the **pericardium**—which is reflected over its whole external surface, as an exceedingly thin layer of connective tissue covered with endothelial cells; this is the **visceral layer** of the pericardium. The outer or **parietal layer** is strengthened by the greater development of its fibrous tissue. The interior of the heart is lined by another serous membrane—the **endocardium**—which has also a fibrous and an endothelial layer. The wall of the heart consists of a special form of muscle already described (p. 24). The heart consists of **two atria** (**auricles**) and **two ventricles**—an atrium and a ventricle on the right, and an atrium and a

ventricle on the left side. These pairs of cavities are very similar on the two sides as regards capacity; each ventricle expels about 60 c.c. of blood per beat, but the left ventricle has much thicker walls than the right. The **right pair** contains **venous,** and the **left pair arterial** blood. In the **fœtus** the right and left atria communicate directly through the **foramen ovale,** but this closes soon after birth.

The heart, in the healthy human adult, makes about 72 beats in a minute; at birth it makes 140, at three years 100, and in old age only about 60, or less. In children and women the number of beats varies more than in men, and the heart beats more rapidly in women than in men. The rate of the heart's action increases slightly in extreme old age. At birth the heart weighs about 24 grammes, or 0·75 per cent. of the body weight. The adult heart weighs about 300 grammes, or 0·45 per cent. of the body weight.

Course of the Circulation.—Starting from the right atrium, the blood passes through the tricuspid valve into the right ventricle; from the right ventricle it is distributed to the lungs through the pulmonary artery; in the lungs the blood is oxygenated. It returns to the left atrium by the pulmonary veins. This is called the **lesser** or **pulmonary circulation.** It must be observed that the blood in the pulmonary artery is *venous*, that in the pulmonary veins *arterial.* From the left atrium the blood passes through the mitral valve into the left ventricle; and from the left ventricle into the aorta, which distributes it to the body. In the capillaries of the system the blood gives up its oxygen and becomes venous; it then passes into the veins and back to the right atrium. This is called the **greater** or **systemic circulation.**

Besides the valves between the atria and ventricles, there are valves at the orifice of the pulmonary artery and of the aorta. These are called **semilunar,** from the shape of their cusps or flaps, of which each valve has three. There are also valves in the systemic veins, especially where these are subjected to intermittent pressure from muscular action (see p. 56).

The Heart's Action.—The movement or circula-

tion of the blood is caused by the **pumping action** of the heart. The two atria contract synchronously and suddenly, and pass the blood which they contain into the ventricles. The two ventricles then contract synchronously, and force the blood into the aorta and pulmonary artery.

The contraction of the atria commences at the orifices of the great veins entering them, and thus prevents the blood from passing back. At the commencement of the contraction of the ventricles, the blood gets behind the atrio-ventricular valves and closes them, so that no blood passes back into the atria.

The force required to propel the blood into the aorta is about five times as great as that required to send it into the pulmonary artery, owing to the greater blood pressure in the former; the wall of the left ventricle is about three times as thick as that of the right.

The contraction of either cavity of the heart is technically called its **systole;** its expansion is its **diastole.** The expression 'systole or diastole of the heart' is, however, commonly used by clinicians when referring to the systole or diastole of its *ventricles*.

The changes which occur between the commencement of one heart-beat and the commencement of the next constitute a **cardiac cycle.** Assuming each heart-beat to occupy $\frac{1}{72}$ of a minute, or about 0·8 of a second, then

The atrial systole = 0·1
The ventricular systole = 0·3 } total systole = 0·4.
The total atrial and ventricular diastole = 0·4.

THE HEART SOUNDS.—Each beat of the heart is accompanied by **two sounds.** They are well described by the syllables *lŭb dŭp*; then follows a **pause,** during which no sound is heard; this lasts nearly the same time as the two sounds, and then the sounds are repeated. During the greater part of the pause the heart is dilating, but the contraction of the atria occurs before the end of the pause, which term has relation to the *sound,* and not to the *action,* of the heart. The long sound, *lŭb,* is called the first sound; it is heard at the beginning of the systole of the ven-

tricles. The second sound, *dŭp*, is heard at the end of the contraction of the ventricles, during the closure of the valves at the mouths of the great arteries.

The **first sound** is ascribed to the following causes: the vibration of the atrio-ventricular valves and chordæ tendineæ during the time they are in a state of tension, the rush of blood through the aortic and pulmonary orifices, and the muscular sound produced during the contraction of the heart muscle.

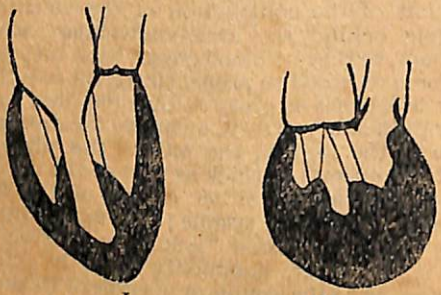


FIG. 12.—DIAGRAM TO SHOW—I., DIASTOLE OF VENTRICLE; II., SYSTOLE OF VENTRICLE.

Observe the position of the valves.

The **second sound** is due to the vibration of the semi-lunar valves, aortic and pulmonary, when their respective cusps meet together.

THE IMPULSE OR APEX BEAT.—Synchronously with the first sound, the apex beat or impulse of the heart is felt in the fifth intercostal space, about an inch inside a line drawn perpendicularly through the left nipple. This is due to the sudden hardening of the heart when it contracts upon the blood, and not to the tilting-up of its apex, as was formerly believed. The heart during contraction becomes more globular, and its base moves downwards, the apex being almost, if not quite, stationary.

The change of form in the heart can be seen in the exposed heart of a frog, and can be demonstrated

in living animals by introducing needles through the thoracic wall. If one be passed into the base, one into the middle, and one into the apex of the heart, that through the base will move most, that through the middle less, and that through the apex will remain more or less stationary.

A **cardiograph** consists of a button or knob which rests upon an intercostal space over the apex beat, the movement of which is transmitted to a lever whose point writes upon a moving smoked surface, producing a tracing—**a cardiogram**.

THE BLOODVESSELS.—The bloodvessels are distinguished as arteries, veins, and capillaries. The **arteries** lead **from the heart,** dividing and subdividing like the branches of a tree, each branch having a smaller cross-section than the vessel from which it arises, although the united cross-section of the branches is always greater than that of the larger vessel. The **veins** lead **to the heart,** and the trunks are larger than their tributaries; but their cross-section is less than the aggregate cross-section of the vessels which form them.

The **capillaries** are intermediate between the smallest arteries (**arterioles**) and the smallest veins (**venules**).

THE ARTERIES are thick-walled vessels, which do not collapse when cut. They contract and empty themselves after death, so that the blood in the body is found in the capillaries and veins, and none in the arteries. The name 'artery' means air-tube, and was given to them, from this circumstance, before the circulation of the blood was understood.

Arteries have **three coats.**

Tunica adventitia.—This is the outer, and is a connective-tissue coat. It is chiefly developed in, and is the strongest part of, the larger arteries. It prevents the artery from being too much stretched when the heart fills it with blood.

Tunica media.—The middle coat is composed partly of thin laminæ of yellow elastic tissue, and partly of non-striated muscle fibres. In the **large arteries** the middle coat contains a large number of **elastic** fibres; in the **small** ones it consists almost entirely of muscle; in moderate-sized **arteries,** like

the radial and ulnar, it is **muscular,** containing, however, a certain amount of **elastic** tissue.

The functions of the middle coat are to keep up a continuous pressure of the blood, and to regulate the amount of blood sent to each organ. The first function is chiefly performed by the elastic tissue, the second by the muscle fibres.

The elastic coat of the arteries is always more or less distended, and this pressure keeps the blood flowing continuously through the capillaries, in the intervals between the successive contractions of the ventricles.

Tunica intima.—The third coat of an artery consists of a tube of **elastic tissue** (not present in the aorta or in the very smallest arteries) lined by a layer of **endothelial cells.** In contact with this layer blood has no tendency to clot.

Both arteries and veins are supplied with small bloodvessels, called **vasa vasorum.** These mostly ramify in the outer, and dip into the middle coat; in the aorta, however, they pass directly outwards from the interior. The muscular fibres of the artery are also supplied with nerves—**nervi vasorum**—which are similarly distributed.

The Veins are comparatively thin-walled vessels, which collapse when they are cut. The aggregate capacity of the veins is about three times that of the arteries. They possess, like the arteries, three coats. The outer and inner are very similar to those of arteries, but the middle contains less muscle and a large amount of fibrous tissue. It is a remarkable fact that any given vein is tougher and stronger than the corresponding artery. The veins serve not only to conduct the blood back to the heart, but the systemic veins are capable of considerable dilation, and contain a reserve supply of blood. As may be seen in the dead body, they are capable of receiving all the arterial blood as well as their own.

The medium-sized veins, especially the veins of the legs, possess **valves,** which prevent any backward flow of the blood. The venæ cavæ, the vertebral veins, and the pulmonary veins, are the chief veins which have no valves.

THE CAPILLARIES are thin-walled vessels, and usually consist of a **single layer** of lozenge-shaped or fusiform **endothelial cells** with sinuous margins, united together by a cement substance. Each cell has a nucleus. The wall of the capillaries is continuous with the endothelial lining of the arteries and veins, which is thus the most fundamental part of a bloodvessel. Here and there on the vessel wall are cells known as **Rouget cells.** These are said by some to have the power of contracting and thus reducing the capillary lumen.

The capillaries form a network in the various tissues, and maintain the same calibre throughout. This network is very close in the lungs; in glands the reticulum is not so close; and in muscles the meshes are oblong and larger. The meshes are widest in the connective tissues, which have no active work to perform.

Exchanges take place between the blood and the tissues, through the capillary walls, of **oxygen,** of **carbonic acid,** and of **nutrient material:** the colourless blood corpuscles also pass through the walls of capillaries and of venules (**diapedesis**). This takes place constantly in inflammation. Coloured blood corpuscles have also, although less often, been observed to pass through the capillary wall.

THE PHYSICAL PHENOMENA OF THE CIRCULATION.

BLOOD PRESSURE.—Every fluid tends to flow from a place of higher to a place of lower pressure. During the contraction of the left ventricle the pressure exerted upon the blood it contains is greater than the pressure of the blood in the aorta; hence the blood flows from the heart into the aorta.

All the systemic arteries are kept in a condition of tension by the action of the left ventricle. The tension is produced by the elastic walls of the vessels being put on the stretch by the blood which they contain, and this tension forces the blood out of the larger arteries into the smaller ones, and from these through the capillaries into the veins.

The force which the blood exerts upon the vessel wall at any particular point is termed the **blood pressure.** It decreases continuously in the direction of the stream, and falls suddenly between the smallest arteries and the capillaries. In the veins it continues to decrease, very slowly at first, but more rapidly as they approach the chest, inside which it becomes negative.*

The **blood pressure** in animals is measured directly by means of a **manometer**—a U-shaped tube containing mercury. One limb of the tube is attached to a lateral branch of the artery in which the pressure is to be measured, by means of a non-elastic tube and cannula filled with a solution of sodium carbonate. The blood, acting through this medium, tends to force the mercury up in the distal limb of the manometer. The difference in the height of the mercury in the two limbs of the manometer is equivalent to the arterial pressure.

In the arteries near the heart the changes in pressure corresponding to systole and diastole are very considerable, but tend to die out in the peripheral vessels owing to the cushioning effect of the walls of the large arteries.

Blood pressure in the human subject is measured with a **sphygmomanometer**—*e.g.*, that of **Riva-Rocci.** A hollow bag made to fit round the upper arm is inflated with air until the pulse in the radial artery just disappears (**systolic pressure**). The air pressure is read off by means of an attached pressure-gauge. A more accurate way of determining the blood pressure is to inflate the bag until the radial pulse is obliterated. The chest piece of a stethoscope is now placed over the brachial artery, on the distal side of the armlet. The air is allowed to escape slowly from the bag, and at the *first* appearance of a rhythmic sound heard in the stethoscope the manometer indicates the **systolic pressure.** On continuing to allow the air to escape, the sounds alter in quality and eventually cease. Just before their final disappearance the sounds alter

* The cause of negative pressure will be treated of in the section on Respiration (see p. 80).

from a hard to a soft muffled murmur. The reading on the manometer when this change occurs is taken as representing **diastolic pressure.** In a young adult the average readings are systolic 120 mm., diastolic 80 mm. of mercury. The difference between the two (40 mm.) is called the **pulse pressure.**

Arterial blood pressure depends on—

(1) The pumping action of the heart.
(2) The peripheral resistance in the small vessels, especially the arterioles.
(3) The quantity of blood in the circulation.

The **arterioles** offer considerable resistance to the stream of blood in its onward course to the capillaries; this resistance is controlled by the **muscular coat** of the arterioles. The small arteries are normally maintained in a condition intermediate between contraction and dilation. This is spoken of as **arterial tone.** When the tone of the arterioles is lost, due to relaxation of the muscle in their walls, there is much less resistance to the flow of blood from the arteries to the veins, and the arterial pressure falls. Much of the peripheral resistance is due to the viscosity of the blood.

If the heart's action were invariable, in regard to force and frequency, the pressure of the blood in the larger arteries would vary directly with the peripheral resistance. If the resistance of the small arteries were constant, increased frequency of the heart's action would increase the blood pressure, by sending more blood into the arteries. This would cause a more rapid flow into the capillaries. There would be an increase both in the pressure and the rate of circulation of the blood.

In the normal condition the mean blood pressure varies only within very narrow limits, as the action of the heart becomes more frequent when the resistance in the arterioles is diminished, and less frequent when it is increased. This is known as **Marey's law.**

The normal blood pressure is not altered perceptibly by food, drink, or exercise. Moderate hæmorrhage

does not reduce it, as fluid is rapidly absorbed to make up the normal quantity of blood; but it is reduced by copious hæmorrhage—for a time, at least. Sudden relaxation of the arterial tone at once lowers the blood pressure and produces faintness.

THE PULSE.—Each contraction of the left ventricle

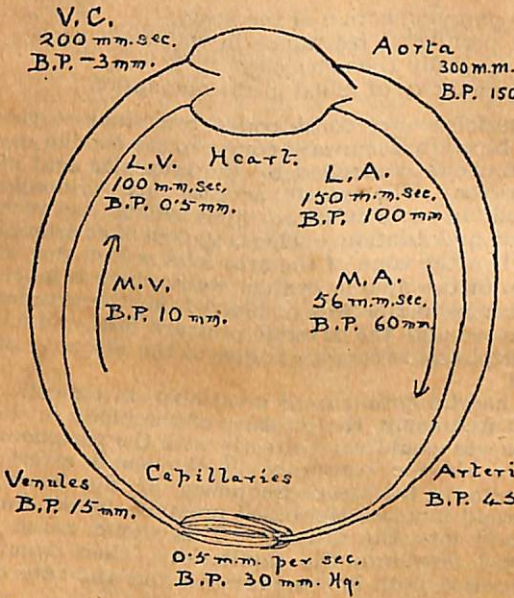


FIG. 13.—DIAGRAM TO SHOW THE BLOOD PRESSURE AND THE VELOCITY OF THE BLOOD STREAM IN DIFFERENT PARTS OF THE CIRCULATORY SYSTEM.

L.A., Large artery; *L.V.*, large vein; *M.A.*, medium-sized artery; *M.V.*, medium-sized vein; *V.C.*, vena cava.

gives rise to a dilation of the systemic arteries (with an increase of blood pressure) which is propagated as a wave towards the smallest arteries. The wave is

the **pulse-wave.** This travels through the arteries at the rate of from 7 to 10 metres a second, that is, about thirty times as fast as the blood flows. The pulse-wave can be accurately investigated by means of the **sphygmograph,** an instrument which consists essentially of a button or pad which is adjusted over the artery, a lever which amplifies the movements of the button, and a moving slip of smoked paper upon which the lever traces a curve representing the pulse-wave.

The pulse-curve, or **sphygmographic tracing,** consists of a nearly vertical upstroke — **anacrotic** or **percussion wave,** followed by a more gradual down-stroke—**catacrotic wave,** interrupted by a second rise —the **dicrotic wave.** This last occurs at the end of

FIG. 14.—SPHYGMOGRAPHIC TRACING OF RADIAL PULSE.

A, Primary or percussion wave; B, pre-dicrotic wave; C, dicrotic notch; D, dicrotic wave.

the systole of the heart, and corresponds with the closure of the semilunar valves. Just before this there is a small **predicrotic wave** due to the vibration in the arterial wall. Point C in Fig. 14 represents the end of systole. The dicrotic wave is more developed when the tension of the arteries is less than normal, and when the contraction of the ventricle is strong and sudden.

The pulse-wave is entirely lost in the smallest arteries and capillaries, except when the former are very much dilated, in which case it extends to the capillaries, and may even become perceptible in the small veins.

THE RATE OF THE CIRCULATION.—The rate of flow depends on the amount of blood discharged from the heart, on the diameter of each vessel, and on the total cross-section of the vessel bed at any given part.

For instance, the rate of flow in the aorta is about 12 inches a second, the aggregate cross-section of the systemic capillaries is about 600 times as great as the cross-section of the aorta; hence the flow is 600 times less rapid, or about $\frac{1}{50}$ of an inch in a second. As the branches of an artery added together always have a larger cross-section than the trunk, the circulation becomes slower and slower as the current approaches the capillaries. In the veins, on the other hand, the rate of flow increases towards the heart, because there also the trunks have a smaller cross-section than the sum of the capillaries. The rate of the circulation in animals is measured experimentally by several instruments, of which **Ludwig's stromuhr** is one of the best.

The time taken by the blood to circulate through the vessels has been determined in animals by injecting a solution of methylene blue into one jugular vein and observing how long it takes to complete the circulation and appear in blood drawn from the other jugular. By this means it has been found that the time of the circulation is about 27 heart-beats.

WORK OF THE HEART.—The work of the heart during contraction may be roughly calculated by multiplying the output of the ventricles (Q) by the resistance (R), against which the blood has to be forced. The resistance is usually expressed in mm. Hg., and to reduce the calculation to gram-metres of blood, it is necessary to multiply this factor by the density of mercury relative to blood—12·8.

Assuming the output of each ventricle to be 60 c.c., and the mean pressure in left ventricle to be 110 mm. Hg., and that in the right ventricle as 20 mm. Hg., then—

Left ventricle, $W = Q \times R$ $60 \times 0{\cdot}11 \times 12{\cdot}8 = 84{\cdot}5$ g. metres.
Right ventricle, $W = Q \times R$ $60 \times 0{\cdot}02 \times 12{\cdot}8 = 15{\cdot}5$ g. metres.
Total work of heart $84{\cdot}5 + 15{\cdot}5 = 100$ gram-metres.

This calculation does not take into account the work necessary to impart the velocity to the blood, but this is negligible.

THE CAPILLARY CIRCULATION should be watched in the web of a frog's foot with the aid of a microscope.

In the smallest capillaries the corpuscles are sometimes seen flowing through the vessels in single file with great regularity. Sometimes the corpuscles get blocked at the entrance to a vessel, which then for a time is filled only with plasma. The corpuscles frequently alter their form in escaping from such a block, or in turning corners, and show considerable elasticity. In the largest capillaries or smallest arteries the coloured corpuscles are seen only in the centre of the vessel—the axial stream—surrounded by a layer of plasma—the inert layer—in which colourless corpuscles are frequently observed moving very slowly or clinging to the walls of the vessel. In the larger arteries the stream moves in jets corresponding with the pulsations of the ventricle. This movement extends into the capillaries or even the veins when the tone of the small arteries is deficient.

The capillaries vary in size with the quantity of blood which reaches them, but it is now known that they have the power of independently contracting and dilating, and thus act as an important factor in regulating the peripheral resistance. They are dilated by **histamine** and contracted by **adrenaline** and **pituitrin.**

Myocardiac Mechanism and Sequence of Beat.

The muscle of the atria and that of the ventricles are not in direct continuity, due to the interposition of the fibro-cartilaginous ring supporting the atrio-ventricular valves. At the base, however, of the interatrial septum is situated a sensitive tissue known as the **atrio-ventricular node** (A.V. node), which is the commencement of a bunch of fibres called the **atrio-ventricular bundle** (bundle of His). This is composed of a modified form of cardiac muscle, and near the commencement of the interventricular septum it divides into right and left lateral branches. These continue down in the interventricular septum, and by means of terminal ramifications called Purkinje fibres, they convey the stimulus to the papillary muscles and thence to the base of the ventricles. The bundle of His is essentially a *conducting* mechanism, and the

impulse travels along it about ten times as fast as in ventricular muscle.

The contraction of the heart commences at a sensitive tissue called the **sino-auricular node** (S.A. node), situated in the wall of the right atrium between the entrances of the large veins. From here the impulse spreads rapidly over both atria, and reaches the A.V. node. It is then propagated throughout the ventricles by the A.V. bundle and its branches. Due to the course of the latter, the papillary muscles begin to contract before the base of the ventricles and thus the chordæ tendineæ are tightened at the beginning of ventricular systole. This prevents the cusps of the valves being everted into the atria by the high interventricular pressure developed before the blood flows into the aorta and pulmonary artery.

Owing to the fact that in the normal heart the impulses always commence at the S.A. node, which therefore determines the rhythm of the heart, this node has received the name of the **pace maker.**

Heart block is due to some defect in either the S.A. node or in the conduction mechanism of the heart. In the former (S.A. block), the impulse fails to pass out of the node and so a complete cardiac contraction is missed, that is, neither atria nor ventricles contract. This type is usually due to marked vagal action exercising excessive inhibition over the node.

Disease or damage of the A.V. bundle or of any of its ramifications may result in (*a*) delayed or imperfect conduction of impulse from atria to ventricles, or (*b*) in complete blockage of conduction. The first lesion gives any of the types of **partial heart block,** the second causes **complete heart block.** If the injury be to one of the branches of the bundle, the result is **bundle branch block.**

Partial heart block may be of three degrees.

(*a*) *Delayed conduction,* where conduction time from atria to ventricles is abnormally prolonged.
(*b*) *Occasional dropped beat,* where an occasional atrial contraction fails to be followed by a ventricular contraction.

(c) *Regular dropped beat,* where the atria contract at a regular rhythm but the ventricles fail at regular intervals to respond to the atrial stimulations. The ratio of atrial to ventricular contraction determines the type of this degree, viz., 2 to 1; 3 to 2; 4 to 3; and so on.

In complete heart-block there is complete dissociation of atrial and ventricular contractions. The atria contract normally, followin g S.A. node timulation (rate about 72), while the ventricles follow their own irritability (independent of node and atria) at a rate of 40 or less.

In bundle branch block the two ventricles contract at the same rate as the atria, but not simultaneously with each other.

The existence of heart-block may be deduced from a simultaneous record of the **venous pulse in the neck** and of the arterial pulse. Atrial beats are registered on the venous pulse, ventricular on the arterial. It may also be registered by means of the **electrocardiogram,** obtained with the help of Einthoven's **string galvanometer.** A electrocardiogram of the normal heart shows a series of waves, marked *P, Q, R, S, T.* The wave *P* is due to the atrial contraction, *Q* to *T* to the ventricular contraction.

In an electrocardiogram taken from a case of heart-block, each atrial contraction is as a rule recognisable, and the want of correspondence between these and the ventricular contractions is readily apparent (Fig. 16, II.). In delayed conduction the *P* to *R* interval is markedly prolonged.

Fibrillary contraction of the ventricles may be produced by ligature of the coronary arteries, by strong electrical shocks or by injury to certain parts of the heart. In this condition, which is generally fatal, the muscle fibres contract, not in a co-ordinated fashion, but separately and irregularly, so that the surface of the ventricles has the appearance of an irregularly twitching mass. The application of the string galvanometer to clinical cases has brought to

light the fact that in some individuals the atria suffer permanently from fibrillation (Fig. 16, III.).

PERFUSION OF THE HEART.—By tying a cannula into the ascending aorta and perfusing warm Ringer's

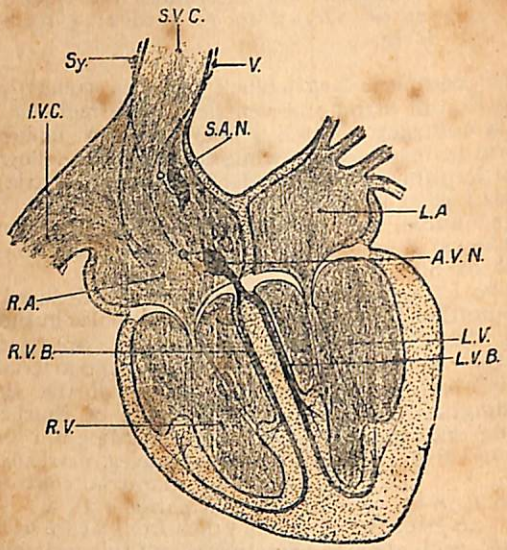


FIG. 15.—DIAGRAM OF HEART SHOWING THE CONDUCTING BUNDLES.

A.V.N., Atrio-ventricular node, with *R.* and *L.V.B.*, right and left atrio-ventricular bundles; *S.A.N.*, sino-auricular node; *Sy.*, sympathetic nerve; *V.*, vagus nerve and its branches. *I.* and *S.V.C.*, Inferior and superior venæ cavæ; *R.* and *L.A.*, right and left atria; *R.* and *L.V.*, right and left ventricles.

or Locke's solution through the coronary vessels, the excised mammalian heart may be kept beating for a considerable period. A certain **pressure** of fluid is necessary in order that it may be forced through the coronary vessels. This is one reason why arterial

blood pressure must remain high. The **calcium** salt in the Ringer's solution promotes **systole**, the **potassium** salt promotes **diastole**, the **sodium** salt maintains

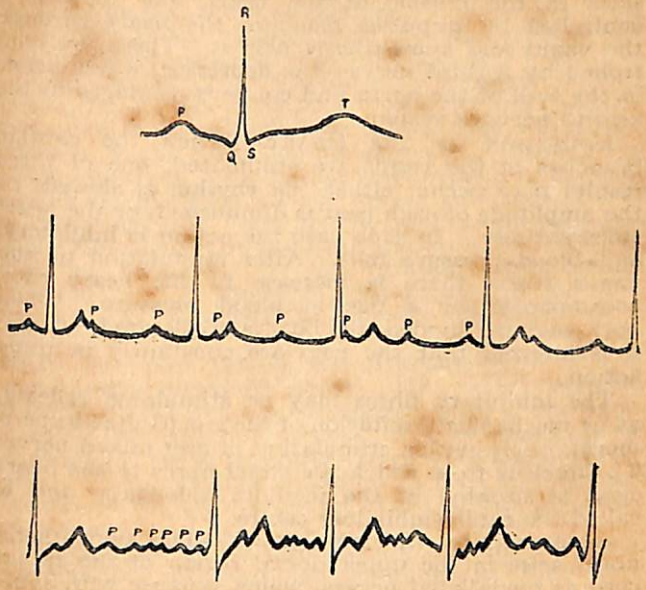


FIG. 16.—ELECTROCARDIOGRAMS, NORMAL AND ABNORMAL.

I. Shows a single response of the normal heart. The wave P is due to the atrium, the waves marked Q, R, S and T represent the ventricular contraction.

II. From a case of complete heart-block. Observe the entire want of correspondence between atrial and ventricular contractions.

III. From a case of atrial fibrillation. The atrium is never completely at rest; its responses, too, are irregular in form.

the **rhythm.** Both dextrose and lipoid substances help to supply energy, though without these the beat is long maintained.

Cardiac Nerves.

Although the power of **rhythmical contraction** resides in the muscle of the heart, the rhythm is **controlled** by impulses reaching the heart through the **vagus** and sympathetic nerves. These are controlled by a third nerve—the **depressor,** which arises in the wall of the aorta and conveys messages to the central nervous system.

Inhibition of the Heart.—When the cardiac branches of the vagus are stimulated, one of three results may occur: either the **rhythm** is slowed, or the **amplitude** of each beat is diminished, or the heart **stops** entirely. In each case the action is **inhibitory,** and blood pressure falls. After stimulation of the vagus *ceases* there is increase in the heart rate, accompanied by a rise in blood pressure. When both vagi are divided, the beat is accelerated, whence it is inferred that the vagi are constantly in tonic action.

The inhibitory fibres may be stimulated **reflexly,** as by mechanical excitation of the gut (Goltz's experiment), or by pathic stimulation of any mixed nerve. The nucleus from which the vagal fibres to the heart arise is situated in the medulla oblongata, and is called the **cardio-inhibitory centre.**

Acceleration of the Heart.—The **sympathetic** fibres arise in the upper dorsal region of the spinal cord as medullated nerves, which synapse with sympathetic nerve cells in the inferior cervical ganglion. Stimulation of these causes **acceleration** and **augmentation** of the beat, after a considerable latent period, which effects continue for some time after the stimulation has ceased. Section of the sympathetic nerves causes slowing—*i.e.*, they are normally in tonic action.

Effect of Drugs on the Heart.—**Atropine** paralyses the effect of the inhibitory nerves, causing quickening and greater force in the heart-beat. It seems to act on the heart muscle.

Acetylcholine has an effect similar to vagus stimulation, and slows the heart. It is antagonised by atropine.

Vaso-Motor Nerves.

The bloodvessels, particularly the arterioles, are supplied with two opposing sets of nerves, the **vaso-constrictors** and the **vaso-dilators.** Collectively these are known as the **vasomotor** nerves, and they belong to the autonomic nervous system (p. 211).

Vaso-Constrictor Fibres.—The vaso-constrictors belong to the sympathetic system, and emerge from the spinal cord as medullated fibres from the second thoracic to the third lumbar segments. These enter the sympathetic ganglia and are distributed as post-ganglionic fibres to all the spinal nerves, and still as pre-ganglionic fibres to the abdominal plexuses. The vaso-constrictor fibres are always in tonic action, and are controlled by the **vaso-constrictor centre** situated in the medulla. Stimulation of afferent nerves may increase the activity of this centre, causing a general rise in blood pressure—**pressor effect**—or (more rarely) may decrease the action of the centre—**depressor** effect. The chief **depressor nerve** is a branch from the **aortic region** of the heart (see p. 68). The occurrence of slow waves on a tracing of blood-pressure—**Traube-Hering waves**—points to a rhythmic alteration of tone in the vaso-constrictor centre, or in the walls of the arterioles themselves.

Adrenaline causes stimulation of the ultimate terminations of vaso-constrictor nerves, thus producing a marked rise in blood-pressure.

Ergotoxine paralyses the terminations of vaso-constrictor fibres, thus causing a fall in blood-pressure.

Vaso-Dilator Fibres, generally speaking, belong to the parasympathetic system, and they may be found in the mixed nerves along with the vaso-constrictors. Stimulation of a mixed nerve usually causes vaso-constriction, but (1) by **slow and weak stimulation,** or (2) by cutting the nerve and allowing it to **degenerate** for a day or two and then stimulating it, the presence of the vaso-dilators can be detected. This latter effect is due to the fact that the vaso-constrictors degenerate earlier than the vaso-dilators.

A few nerves—*e.g.*, the **chorda tympani**, the **nerve of Jacobson**, the **nervi erigentes**—contain vaso-dilator and no vaso-constrictor fibres. Stimulation of a sensory receptor, even after its nerve has been cut, causes vaso-dilatation (**antidromic impulses**). Each sensory fibre at its termination divides, one part going, say, to the skin, the other to the plain muscle of the underlying vessels. Pathic stimulation of the sensory fibres, which brings about a *general vaso-constriction* and rise of blood pressure, by this short **axon reflex** causes **local** *vaso-dilatation*.

Acetylcholine has the effect of stimulating vaso-dilator fibres, and thus produces dilatation of the bloodvessels.

The *vaso-constrictor* nerves may be considered as controlling the bloodvessels throughout the body

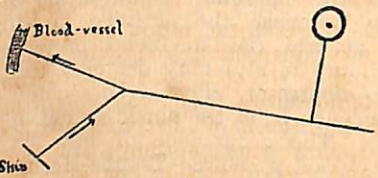


FIG. 17.—DIAGRAM OF AXON REFLEX.

generally, whereas the *vaso-dilator* fibres are affected by local conditions, allowing increased blood supply to the organs specially requiring it.

SPECIAL ORGANS.—There are no vaso-motor nerves to the vessels of the **brain.** The cerebral circulation is dependent upon the general arterial pressure. If this is low the brain circulation is slowed, and faintness may occur unless the pressure is raised. At the bifurcation of the common carotid artery there is a dilatation in its calibre known as the **carotid sinus,** which acts as a regulating mechanism to control reflexly the cerebral circulation. In the wall of this sinus, nerve fibres arise which travel in the glosso-pharyngeal nerve to reach the vaso-constrictor centre. When the general blood pressure rises these fibres are stimulated, and the result of their message

is to *inhibit* the tone of the vaso-constrictor centre. This lowers the blood pressure generally, and thus protects the cerebral vessels. Conversely, when the general pressure tends to fall, and anæmia of the brain is threatened, the message from the carotid sinus has the effect of *stimulating* the vaso-constrictor centre. This raises the general pressure, and so forces more blood through the brain. The **coronary vessels** are supplied with *vaso-constrictor* fibres from the vagus, and *vaso-dilator* fibres from the sympathetic. The blood supply to the **abdominal organs** is regulated by vaso-constrictor impulses passing outwards along the splanchnic nerves, the synapse station being in the solar ganglia. Section of these nerves or temporary paralysis of the ganglia (due to a blow on the abdomen) causes an enormous fall of blood pressure.

METHODS.—Vaso-motor action can be investigated —(1) by simple **inspection** (reddening denotes vaso-dilatation, paling denotes vaso-constriction); (2) by change of **temperature** (with vaso-dilatation a peripheral part, like the hand, becomes warmer); (3) by recording the **venous outflow** (vaso-constriction diminishes and vaso-dilatation increases this); (4) by **plethysmography,** or recording the change of volume of an organ—of especial use in connexion with the viscera and the limbs.

THE LYMPHATIC SYSTEM.

Blood plasma, together with some colourless blood corpuscles, escape through the thin walls of the capillaries and irrigate the various tissues of the body. This fluid finds its way, through a distinct system of spaces and vessels, back into the great veins, and so returns into the blood stream as lymph. The **lymph** is a modified form of blood plasma, which has lost a portion of its solids in nourishing the various tissues through which it passes, and which has received the waste materials from the tissues themselves.

Lymph is an alkaline fluid of specific gravity 1·015, which clots when withdrawn from the lymph vessels.

The proteins and salts are those which are found in blood plasma. The **spaces** and **vessels** by which it flows back again into the blood, together with certain glands of peculiar structure (**lymphatic glands**), form the **lymphatic system.**

The lymphatics of the small intestine (**lacteals**) do not differ in structure from ordinary lymphatics. The fluid (chyle) which they contain, however, is white and opaque like milk. It will be treated of in the section on Absorption.

The lymphatics arise in the interstices of the connective tissue of the various organs, possibly as minute irregular branching spaces or clefts, which intercommunicate with each other. The lymph vessels are formed of a single layer of endothelial cells. They differ from blood capillaries in having a large diameter and in varying more in size.

The lymph vessels are gathered up into larger vessels, with swellings at intervals; behind each swelling—that is, on the side nearer to the capillaries —a **valve** is formed by the infolding of the wall of the vessel. These valves are like the valves in the veins, and they occur at frequent intervals throughout the remainder of the lymphatic vessels.

Although the lymph spaces are large, the vessels by which the lymph is collected are far smaller than the veins. All the lymphatic trunks in the body are collected together into two main trunks, the larger of which (**the thoracic duct**) is scarcely greater than a crow-quill; **the lesser thoracic duct,** which collects the lymph from the right arm, and the right side of the head, neck, and thorax, is much smaller. The larger lymphatic trunks have the same structure as the veins.

All the lymphatic vessels, sooner or later in their course, communicate with lymphatic glands. The vessels which bring the lymph to the gland are called **afferent,** and those which carry it on, after it has passed through the gland, **efferent** lymphatics.

A **lymphatic gland** consists of a **reticulum** of adenoid tissue enclosed in a **capsule** of fibrous tissue with some smooth muscle. The capsule is continuous with the outer coat of a group of anastomosing afferent lym-

phatics. It encloses the whole gland, but is drawn in at a point opposite to that at which the afferent lymphatics enter it, so that a depression is formed, called the **hilum.** The efferent lymphatics leave the gland at this point.

The capsule sends numerous incomplete partitions into the interior of the gland (**trabeculæ**), which divide it into a vast number of compartments, so that the whole resembles a sponge. They are lined by an endothelium continuous with the inner coat of the lymphatic vessels, from which a network of protoplasmic threads and branching cells still further divides the gland into a spongy reticulum—**retiform tissue**—in the meshes of which vast numbers of active protoplasmic cells are entangled. This is the **adenoid tissue** already discussed.

In the outer or **cortical portions** of the gland a space exists between the endothelium and the adenoid tissue which contains retiform tissue and lymph only. These spaces are spoken of as **lymph channels,** and are in direct continuity with the interior of the afferent lymphatics.

The inner or **medullary** portion of the gland is completely filled with adenoid tissue arranged in the form of **lymphoid cords,** in which the efferent lymphatics arise, so that the lymph passes into the gland and is distributed through its cortex by the lymph paths, and after filtering through the adenoid tissue, leaves it again by the **efferent lymphatics.** In this way it is brought into relation with the active cells of the adenoid tissue, by which it is prepared, as it were, for readmission to the blood.

The cells of the lymphatic glands undoubtedly remove certain materials from the lymph. Micro-organisms taken up by the lymphatic vessels may set up morbid changes in the glands, where their progress is, to some extent at least, arrested.

The lymph after passing through the glands is also richer in lymph-corpuscles, and it is certain that many of the blood lymphocytes originate thus in the lymphatic glands.

CHAPTER VIII

RESPIRATION

RESPIRATION means the taking in of **oxygen**, the union of oxygen with carbon to form carbonic acid gas, and the elimination of the **carbonic acid.** Oxygen also unites with hydrogen to form water, which may be eliminated either by the lungs, the skin, or the kidneys. A distinction must be drawn between the actual gaseous interchange in the tissues—**internal respiration**—and the exchange of gases which takes place between the venous blood and the alveolar air —**external respiration.**

THE ORGANS OF RESPIRATION.

THE ORGANS OF RESPIRATION are the lungs, the air-passages, and the thoracic walls.

THE AIR-PASSAGES consist of the respiratory tract, of the nasal fossæ, and of the pharynx, larynx, trachea, and bronchi. The respiratory tract of the **nasal fossæ** is lined by a thick vascular mucous membrane, the extent of which is considerably augmented by the reduplications covering the inferior turbinate bone. It is kept moist by the secretion of numerous glands, and serves the purpose of warming the inspired air, at the same time saturating it with aqueous vapour.

The **larynx, trachea,** and the larger **bronchi** are very similar to each other in their microscopic structure; they are tubular, and their walls consist of three coats —an external connective-tissue coat; a middle coat, composed of hyaline cartilage, fibrous tissue, and muscular fibres; and an internal or mucous membrane, which is united to the middle coat by a layer of loose connective tissue called the submucosa.

MUCOUS MEMBRANES.—This term is applied to the lining membranes of those cavities of the body which are provided with external outlets, and of their glandular diverticula. They are constantly in contact either with air or food introduced from without, or with some secretion or excretion. Their surfaces

are protected by a more or less tenacious fluid secreted by glands situated in their substance, or by some of the epithelial cells with which they are covered. This fluid owes its tenacity to the presence of **mucin**, and is called 'mucus'; it also contains numerous cells, similar to the colourless corpuscles of the blood—**mucous corpuscles.**

A **mucous membrane** consists of an **epithelium**, a **basement membrane**, a **corium** or fibrous layer, and a **submucous** reticulum of **connective tissue.**

The **respiratory** mucous membrane is lined with **columnar ciliated epithelium** resting upon a layer of basal cells, as far as the smaller bronchial tubes, where the epithelium is first reduced to a single layer of columnar ciliated cells. It then becomes cubical, and afterwards, in the terminal **bronchioles** and **alveoli**, it consists of a **single layer** of **pavement cells without cilia.**

The **vocal cords** are an exception to the above, being covered with **stratified squamous epithelium.**

The function of the cilia is to keep the secretion of the air-tubes moving towards their orifices, and thus to assist the removal of dust and other foreign particles which find admission with the air, and become entangled in the mucous secretion.

The epithelium rests upon a **basement membrane.** The **corium** consists of a reticulum of fibres, dense next the basement membrane, and gradually becoming looser, and passing insensibly into the submucous connective tissue. It is richly supplied with capillaries, which are connected with arterioles and venules that ramify chiefly in the submucous layer. The corium is especially rich in **lymphatic channels** and **adenoid tissue.** This lymphoid tissue forms small separate masses in various parts of the mucous membrane, which are called solitary glands, or follicles.

The mucous membrane, also, is studded with **secreting glands.** Those of the respiratory tract are **compound racemose** glands; some secrete a mucous, others a thin serous fluid, with which the surface of the mucous membrane is kept moist. These glands are essentially involutions of the mucous membrane: they

consist of a basement membrane continuous with that of the mucous membrane itself. This forms a branching tube—the **duct**—which ends in little pouches called **acini.** These are bound together by connective tissue, and form the lobules of the gland. The ducts are lined by **columnar epithelial** cells, and the acini by **cubical** or spheroidal cells; these are the secreting cells (glandular epithelium). The exterior of their

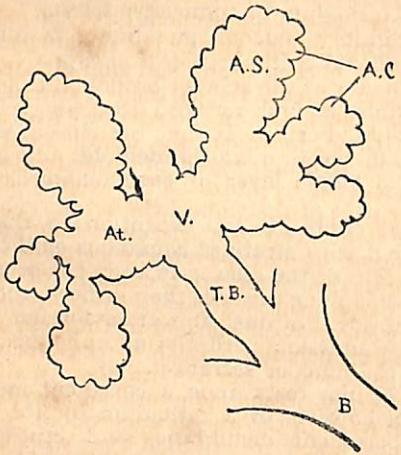


FIG. 18.—DIAGRAM OF TERMINAL BRONCHIOLE.

B., Bronchiole; T.B., terminal bronchiole; V., vestibule; At., atrium; A.S., air-sac; A.C., air-cells or alveoli.

basement membrane is covered by a plexus of capillaries. The glands extend into the submucous coat of the trachea and bronchi, and many even pierce the entire wall of the tube, appearing as lobular projections on its outer surface.

Immediately beneath the outer layers of the corium, a layer of **non-striated muscle cells** is conspicuous in the medium-sized and smaller bronchi; this is the **muscularis mucosæ.** The submucous layer consists

of loose connective tissue, which has an abundance of elastic and fibrous tissue intermixed with it.

The **middle coat** of the **larynx, trachea,** and **larger bronchi** consists of **hyaline cartilage** and fibrous tissue. The larynx has also striated muscles, by which the cartilages are moved upon each other; these are concerned in respiration, but mainly in modifying the condition of the vocal cords for the purpose of producing sounds (the voice).

The trachea and large bronchi have the cartilage in the form of **incomplete rings;** the opening in the ring is closed with fibrous tissue and **non-striated muscle.** In the smaller bronchi the cartilage exists in the form of irregular plates, and in the smallest it is altogether absent; in these, however, the middle coat is represented by a distinct layer of non-striated muscle fibres (innervated by fibres of the vagus) which form the greater part of the wall of the tube. The mucous membrane is reduced to a basement membrane, with a single layer of flat pavement cells on its inner surface, and the outer coat consists of a delicate reticulum of connective tissue.

The very smallest divisions of the bronchi are known as **terminal bronchioles.** Each of these consists of a **vestibule,** into which open a number of dilatations, known as **atria,** which communicate with the **air-sacs.** The walls of the air-sacs, as well as those of the vestibule and atria, are studded over with **air-cells** or **alveoli,** in which latter compartments the gaseous interchanges between the blood and the alveolar air take place.

The outside of the air-sacs is covered by a very close network of small **capillaries,** uniting the pulmonary artery and vein; only a single layer of capillaries exist between each pair of adjacent air-cavities, so that the blood in these vessels has air on both sides of it. The air-sacs are lined by a delicate pavement epithelium, and are bound together by a very fine network of **elastic** fibres.

THE PLEURÆ are a pair of serous sacs, one enclosing each lung; each pleura consists of a pulmonary or **visceral,** and a **parietal** portion, and these are con-

tinuous with each other at the root of the lung. The parietal layer is closely applied to the interior of the wall of the thorax, except where it is reflected inwards, and bounds the **mediastinum**; the pulmonary layer is intimately connected with the surface of the lung and the connective tissue between the lobules and lobes of the organ. The visceral layer is thinner than the parietal; both are connective-tissue membranes, **rich in lymphatics.**

The cavity of the pleura is lined by **pavement endothelium.** Between the cells there are numerous minute openings—**stomata**—which communicate with the lymphatic channels in the membrane. The stomata are surrounded by rings of small cubical cells, six or eight around each opening.

The Physical Phenomena of Respiration.

The subdivision of the air passages in the lungs into bronchioles and the terminal air-sacs may be likened to the subdivision of the trunk of a tree into branches and smaller branches and their terminal leaves. Just as every leaf is in direct physical contact with the trunk, so has every air-sac an uninterrupted air passage to the trachea. The walls of the lungs are very elastic, and the air-sacs are maintained patent enclosed within an air-tight cavity—the thorax. Collapse of the elastic wall, and expulsion of a large portion of the air which the lungs contain, is prevented by the external air having no access to the cavity of the chest except by passing into the interior of the lungs.

A puncture in the chest wall, which penetrates and admits air into the pleural cavity, gives rise to the immediate collapse of the lung to about one-fourth of its normal magnitude

The Chest Wall is resilient; in its normal condition it neither tends to expand nor to contract at the end of an ordinary expiration. It is then in a condition of equilibrium.

The Respiratory Act is ordinary, when breathing is accomplished without effort, and occurs from 16 to

17 times a minute. It consists of an active **inspiration**, during which the thoracic cavity is augmented by about 500 c.c., by the contraction of the muscles of ordinary inspiration.

This augmentation is followed by a collapse of the thoracic wall, partly due to gravity and partly to its resiliency acting with the elastic lungs, which restores equilibrium, and expels a portion of air from the lungs. This is the **expiratory act.** It is purely **passive.**

The more important **muscles** of **ordinary inspiration** are the diaphragm, the external and part of the internal intercostals, the levatores costarum, and the serratus posterior superior.

In the condition of rest the **diaphragm** forms a double dome convex towards the thorax. Its **central tendon** is attached to the pericardium, and is practically fixed, but is lower than the relaxed muscular portion, which is drawn up around the central tendon and brought into close proximity with the lower ribs by the negative pressure in the thoracic cavity. It is pressed upwards by the positive pressure in the abdomen.

During the contraction of its muscle fibres the **lateral portions** of the diaphragm **descend,** and are withdrawn from the lower ribs; hence the **cavity of the thorax is enlarged.**

At the same time the ribs are *everted*, and their anterior extremities are raised, by the levatores costarum and intercostal muscles. As the ribs are placed obliquely, with their anterior extremities lower than their posterior, these movements increase both the transverse and the antero-posterior diameters of the chest, and so increase the capacity of the thoracic cavity.

Tidal Air.—The air which passes in and out of the chest during ordinary respiration is called **tidal air.** This in a healthy adult male amounts to about 500 c.c.

During **forced inspiration** and **expiration** a much larger quantity of air is changed by each act, as the capacity of the chest can be increased and diminished by about 3,000 c.c. more than in ordinary respiration.

so that about 3,500 c.c. of air are changed. The whole amount of air which can be displaced in this manner is termed the **vital capacity** of the lungs.

The air which can be taken in, beyond that normally inspired in quiet breathing, is called **complemental air** (1,500 c.c.); that which can be expired after a normal expiratory movement, **supplemental air** (1,500 c.c.).

The lungs contain a considerable quantity of air even after the deepest expiration, averaging at least 1,000 c.c. This is spoken of as **residual air,** and only a part of this is expelled after death, even when the thorax is opened and the lungs collapse.

INTRAPULMONIC PRESSURE.—The interior of the lungs is in free communication with the external atmosphere through the medium of the windpipe. During inspiration air flows in, and as it passes only from a region of higher to one of lower pressure, it follows that during inspiration the air-pressure within the lungs (**intrapulmonic pressure**) is slightly less than atmospheric. The converse holds in expiration. At the pauses between the two acts the intrapulmonic pressure is atmospheric, and no flowing movement of air takes place.

INTRATHORACIC PRESSURE.—The lungs being elastic and being constantly kept in distension by the intrapulmonic (*i.e.*, atmospheric) pressure, it follows that the full pressure of the atmosphere cannot act through the lungs upon the interior of the thoracic wall, but is reduced by an amount equal to the elastic force of the distended lungs. This less than atmospheric or **negative pressure,** to which all the extrapulmonic organs of the chest are subjected, is maintained by the rigidity of the thoracic wall. When this is punctured, the air immediately rushes in, and the lung collapses.

Since the lung is more stretched during inspiration, and more of the atmospheric pressure is used up in distending it, the intrathoracic pressure becomes less still. Even during expiration it is lower than atmospheric pressure.

Voice and Speech.

Voice.—When air is driven from the chest, and the vocal cords are approximated, rendered parallel, and put on the stretch, a sound is produced—the voice, the pitch of which depends on the **tension of the vocal cords.** The vocal cords vibrate and render the stream of air intermittent; the more rapid, the higher the pitch. The muscles of the larynx are divided into **extrinsic** and **intrinsic.** The intrinsic muscles fall into the following groups according to the effects of their contraction upon the vocal cords: (1) **abductors,** (2) **adductors,** (3) **those increasing tension.** The adductors are the most numerous. For a description of these muscles and their attachments to the cartilages of the larynx the student must be referred to his textbook of anatomy. All are supplied by the **inferior laryngeal** branch of the **vagus** nerve (the fibres of which come from the spinal accessory) except the **crico-thyroid,** which is supplied by the **external** branch of the superior laryngeal. The **mucous membrane** of the larynx is supplied by the **superior laryngeal** branch of the **vagus.**

Increased tension or diminution in length of the vocal cords increases the number of vibrations, and raises the pitch of the note produced. The loudness depends on the force with which the air is expelled through the rima glottidis.

The quality of the voice arises from secondary or superimposed vibrations—harmonics to the fundamental note; the strength and nature of these depend upon the form and dimensions of the mouth, pharynx, and air-passages.

Speech consists of modified voice and articulate sounds produced by movements of the palate, tongue, and lips.

The Nervous Mechanism of Respiration.

It is essential for the efficient ventilation of the lungs that the muscles of inspiration should act in co-operation with each other. This is assured

through the mediation of a co-ordinating centre known as the **respiratory centre,** which discharges rhythmic impulses to the *nerves* which supply the muscles of inspiration. There are two such centres situated one on each side of the floor of the fourth ventricle near the calamus scriptorius. Although, to a certain extent, their activities are capable of being modified by the will, they are essentially involuntary and **automatic** in their action. The destruction of this portion of the nervous system causes the immediate cessation of the respiratory movements, and consequent death from asphyxia.

The **efferent impulses** are distributed mainly to the facial, vagus, phrenic, and intercostal nerves, and these in turn innervate the muscles of inspiration. The facial nerve is not much concerned in ordinary respiration in man; a slight elevation of the alæ nasi sometimes occurs in inspiration, but it is brought into play in laborious respiration, and in some animals under normal conditions.

The activity of the respiratory centre is modified and controlled by the action of afferent nerves and by the H-ion concentration of the blood, so that the respiratory rhythm acquires a **reflex** character, which may even mask the automatic nature of the act.

THE NERVOUS CONTROL OF RESPIRATION.—The more important nerves modifying the activity of the respiratory centre are those conveying impulses from the higher centres, the lungs, the skin, and the carotid sinus. The inhibiting effect of the higher centres ensures the smoother working of the centre, thus preventing the 'gasping' type of inspiration. The **vagus nerves** convey from the lungs two kinds of fibres, those which *stimulate* inspiration and those which *arrest* inspiration. When one vagus nerve in an animal is divided, the respirations become deeper and less frequent; the effect is far more marked, however, when both vagi are divided. If the central portion of the divided vagus be stimulated, the respirations may become more frequent and shallower or may be arrested altogether. These modifications of respiratory rhythm by afferent stimulation are

best shown, however, when the receptor organs (in the lung) of the intact vagus are stimulated by artificial inflation (**positive ventilation**) or deflation (**negative ventilation**) of the lung tissue. Inflation excites expiration, deflation excites inspiration.

Nevertheless it has been shown in animals that the respiratory rhythm is due to automatic discharges of nerve impulses from the medulla, since the respiratory movements of the nostrils continue to recur regularly when the medulla is separated from the spinal cord, the vagi, and the brain; and these movements are increased by the circulation of blood which is venous, rich in CO_2, and deficient in O_2, through the medulla. It is probable that the action of the vagus nerves tends to render the respiratory act more frequent by facilitating the discharge of nerve impulses from the medulla, and that the afferent impulses, which travel up the vagus and modify the respiratory rhythm, are started in the lungs from the mere mechanical expansion and contraction of the air-cells. It is probable also that the stimulus which originates them is increased by the accumulation of blood in the pulmonary capillaries, which is one of the attendant phenomena of insufficient oxygenation of the blood.

Fibres run in the superior laryngeal nerves which are distributed to the mucous membrane of the larynx. Stimulation of the central end of the superior laryngeal nerve gives rise to cessation of inspiration, and then to violent expiratory efforts, and the same result is produced by the entrance of foreign bodies or irritating gases into the larynx.

Not only is the respiratory act rendered more frequent by the action of the vagi, but the stimulation of the **sensory nerves** of the surface of the body both accelerates and intensifies the movements of ordinary respiration. A familiar example of this occurs when cold water is suddenly applied to the skin.

There is evidence that an increase in the blood pressure in the **carotid sinus** will reflexly diminish the respiratory rate; a fall in the pressure increases the rate.

The Chemical Regulation of Respiration.

Although the afferent nervous stimuli play an important part in the regulation of respiration, yet it is the gases of the blood that ordinarily are responsible for the discharge of impulses from the respiratory centre. An increase of CO_2 causes increased breathing or **hyperpnœa**. This is due to a rise in the *hydrogen ion* concentration of the blood. This concentration, which is kept amazingly constant, is determined by the *ratio* between the free and the combined CO_2, which should be present in the proportions, $\frac{H_2CO_3}{NaHCO_3} = \frac{1}{20}$. Anything which increases the free CO_2 raises the H-ion concentration. This stimulates the respiratory centre to greater activity, increasing both the rate and depth of respirations; the excess of CO_2 is flushed out and the reaction of the blood is once more adjusted, the respiratory movements returning to normal. Conversely, if the above ratio should become less than 1 : 20, the activity of the respiratory centre will be diminished, CO_2 will gather in the blood, increasing the H-ion concentration until once again the centre functions normally.

The amount of the CO_2 in the blood is related to the CO_2 content of the alveolar air, and this sensitivity of the respiratory centre maintains the alveolar CO_2 at a constant level. This level is constant for each individual, but it varies in different men. An average figure is 5·5 per cent., but it may range from 4·5 to 6·2 per cent. During exercise the CO_2 content of both the blood and the alveolar air rises, but the increased ventilation of the lungs brings them back to normal. This is the explanation of the breathlessness which follows hard manual work.

Lack of O_2 in the arterial blood or **anoxemia** also acts, although to a less degree, on the respiratory movements. Its effect varies. If the deficiency is slight it stimulates, if great it inhibits. Anoxemia may be produced either by O_2 being gradually used up (as in a closed chamber), or by ascending to high altitudes. In the latter connexion it plays an im-

portant part in the production of **mountain sickness,** with its concomitants of headache, nausea, confusion of ideas, and muscular inco-ordination. The hyperpnœa produced is not here due to an increased CO_2 tension, but to the oxygen deficiency. The excessive ventilation of the lungs flushes out the CO_2, and the tension of this gas in the blood *falls.* This lowers the H-ion concentration and breathing then tends to slow or stop. The acclimatisation which occurs in prolonged anoxemia results from the kidneys excreting the excess of alkali, and so raising the hydrogen ion concentration to normal values. There is also a relative increase in the number of the blood corpuscles, due to a diminution of the circulating plasma. This increases the oxygen-carrying power of the blood. Lack of carbon dioxide, or 'acapnia,' does not play any part in the production of mountain sickness.

Although variations in the O_2 and CO_2 content of the blood produce the effects enumerated above, they are not due *entirely* to the action of these gases upon the respiratory centre alone. It has been shown that these gases affect also the **carotid sinus,** and this in turn acts upon the respiratory centre. An increase in the H-ion concentration of the blood, or a deficiency of oxygen, stimulates the sinus to send out impulses which reflexly increase the activity of the respiratory centre. Conversely, a lessened CO_2 content or a reduced H-ion concentration in the blood passing through the sinus reflexly inhibits the respiratory movements. It is also of interest to note that when, under experimental conditions in animals, the respiratory centre is cut off from all impulses from the carotid sinus, a deficiency of oxygen in the blood *depresses its activity,* and breathing is slowed. It will be seen, therefore, that *anoxemia,* by its direct action on the centre, slows respiration, indirectly through the carotid sinus it stimulates respiration. These opposing effects thus offer an explanation for the variable respiratory responses observed in oxygen lack.

Apnœa.—If the lungs are over-ventilated, either artificially or by breathing more rapidly and deeply

than normally, an excess of CO_2 is flushed out of the lungs, producing a condition known as **acapnia.** This lack of CO_2 lowers the tone of the respiratory centre, which ceases to function, and breathing stops. This is called **apnœa.**

SOBBING consists essentially of a series of short convulsive inspirations followed by a long expiration; whilst laughing is a series of short expirations followed by a long inspiration. The characteristic sounds are due to the condition of the vocal cords.

SIGHING is a long inspiration followed by a shorter but more rapid expiration; it is frequently the result of insufficient respiratory movement or of breathing vitiated air, although it may be due to mental conditions akin to those which produce sobbing.

HICCOUGH.—A reflex spasmodic or convulsive contraction of the diaphragm, usually due to irritation of the branches of the pneumogastric nerve which supply the stomach; it is rather a pathological than a physiological condition. In extreme nervous depression it is frequently a grave symptom.

COUGHING AND SNEEZING are expiratory efforts reflexly produced by irritation of the air-passages, and are the natural means by which foreign bodies or irritating substances are expelled from them; both are expiratory efforts augmented by the closure and sudden opening of the rima glottidis.

ASPHYXIA.—The deprivation of the respiratory centre of oxygenated blood gives rise to asphyxia. The three following stages succeed each other when the deprivation is continuous:

First Stage: Inspiratory and expiratory movements become deeper and more rapid—**hyperpnœa**; this changes to convulsive breathing—**dyspnœa.**

Second Stage: The increased movements of dyspnœa are succeeded by convulsive and irregular breathing, in which expiratory movements are most marked, and eventually by general convulsions of all the muscles of the body.

Third Stage: Exhaustion. In this stage there is general insensibility, coldness, blueness of the surface, and exhaustion of the nervous system; an occasional

long-drawn but feeble inspiratory effort is made, but these gradually die out as death supervenes.

The **blood pressure** rises rapidly during the first and second stages, and falls as rapidly in the third. The lungs, the right side of the heart, the pulmonary artery, and the systemic veins, become at the same time gorged with venous blood.

It must be noted that frequently there is no clear demarcation between the above stages, the one running imperceptibly into the other.

The Relations between Respiration and Circulation.

As the heart and great vessels, as well as the lungs, are contained within the thorax, they are subject to alterations of pressure when its cavity is enlarged during inspiration. As a result of the elasticity of the lungs, at the end of inspiration the intrathoracic pressure is much less than the pressure of the atmosphere. During inspiration, therefore, the heart and vessels tend to expand—the thin-walled veins much more than the arteries—and blood will be sucked into the veins and so into the atria, and on into the ventricles. The increased inflow of blood into the right atrium will accelerate the rate of the heart (**Bainbridge reflex**). Some blood will also be pressed upward into the great veins by the descent of the diaphragm, as this increases the intra-abdominal pressure. At the commencement of **inspiration** the lungs and their capillaries are enlarged owing to the negative pressure in the thorax, the capillaries will hold more blood, and so less blood will flow into the left atrium and on into the left ventricle. *Arterial blood pressure*, therefore, *does not rise until after inspiration has commenced.* At the commencement of **expiration** there is a great inflow of blood from the pulmonary veins to the left atrium and ventricle. The blood pressure is therefore still high at this period, falling during the remainder of expiration.

Chemistry of Respiration.

The inspired air contains about 21 per cent. of oxygen, 79 per cent. of nitrogen and traces of CO_2.

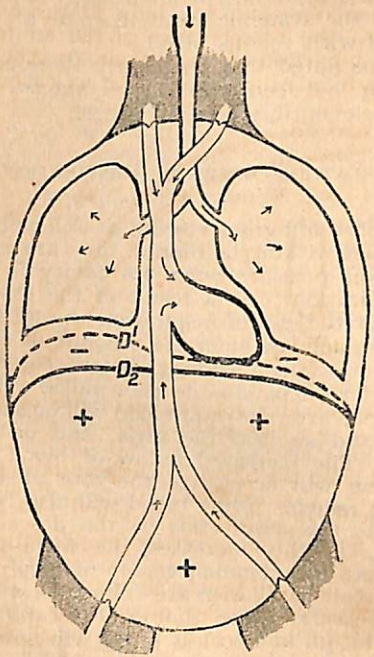


FIG. 19.—DIAGRAM TO ILLUSTRATE RELATION BETWEEN RESPIRATION AND CIRCULATION.

During inspiration the diaphragm moves from D^1 to D_2 position, causing a lessened intra-thoracic (-), and an increased intra-abdominal pressure (+).

Before it is expired it is altered in composition, somewhat reduced in quantity, and warmed.

The expired air contains only 16 per cent. of oxygen,

so that every **100 volumes of tidal air loses about 5 volumes of oxygen**; this passes by diffusion into the alveoli of the lungs. About 4·4 per cent. of carbon dioxide is added to the tidal air, which diffuses into it from the alveoli. As less carbon dioxide is added than oxygen removed, the bulk of the air expired, measured at the temperature of the air inspired, is reduced. A portion of the oxygen absorbed is therefore excreted in other ways than as carbon dioxide

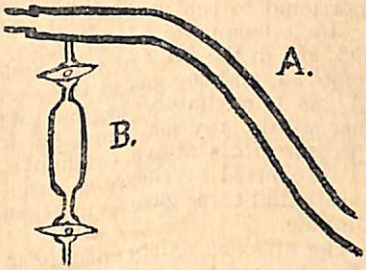


FIG. 20.—APPARATUS FOR THE COLLECTION OF A SAMPLE OF ALVEOLAR AIR.

eliminated from the blood by the respiratory function. The quotient $\frac{CO_2 \text{ expired}}{O_2 \text{ absorbed}}$ is called the **respiratory quotient.** The factors affecting this are fully discussed in Chapter XI.

COMPOSITION OF THE AIR IN THE PULMONARY ALVEOLI.—The respiratory movements do not affect the composition of alveolar air so markedly as they do that of the tidal air.

The composition of the air in the alveoli remains wonderfully constant in the same individual. **Alveolar air** contains about 14 per cent. oxygen, 5·5 per cent. carbon dioxide and 80 per cent. nitrogen.

A sample of alveolar air can be obtained by the following method: A person breathes into a long wide rubber tube (Fig. 20, A), the end of which is either open to the air or opens into a spirometer. At the

end of a *very* deep expiration the subject closes the mouthpiece of the tube with his tongue. A sample of the expired (alveolar) air is drawn into the collecting tube, B, which is then closed, and the contained gas can be analysed.

GASES OF THE BLOOD.—The blood contains gases. These are partly **dissolved** and partly **in chemical combination.**

A gas cannot remain in solution in a liquid unless the same gas is present over the surface of the fluid. The amount dissolved in a given amount of fluid is directly proportional to the pressure of the gas over the surface. In a lemonade bottle there is a high pressure of CO_2 gas in the neck of the bottle. When the cork is removed, and the gas in the neck escapes, the dissolved gas immediately begins to escape as well. In other words, any gas must be driven into solution by pressure from above (without), and that pressure must be exerted by the *same gas.*

In the blood we find three gases—nitrogen, oxygen, and carbon dioxide.

Nitrogen.—The nitrogen exists entirely in solution. When blood is subjected to a reduced pressure under a bell-jar, nitrogen comes off, *exactly* in proportion to the reduction in pressure. On the other hand, when atmospheric air is pumped into a receiver containing blood, nitrogen goes into solution, again in proportion to the pressure. The blood in the lungs being freely exposed to the alveolar air, takes up nitrogen in proportion to the pressure of nitrogen in the alveoli. As no free nitrogen combines with the tissues, the nitrogen content is always the same both in arterial and venous blood. It is increased in caisson workers, who work under increased atmospheric pressure, and is diminished in high altitudes.

Oxygen exists partly in solution and partly in chemical combination. The part in solution obeys the same laws as those just mentioned in connexion with nitrogen. The amount in solution is small (about 0·4 volume per cent.). Arterial blood will, however, give off as much as 18·5 volumes per cent.

of oxygen when exposed to a Torricellian vacuum. Therefore the bulk of the oxygen in the blood is in chemical combination, and this is all contained in the red corpuscles, being combined with the hæmoglobin to form oxyhæmoglobin (see also p. 45). *The amount of oxygen so combined does not come off in proportion to the reduction in pressure.*

Carbon dioxide, like oxygen, is partly in solution and partly chemically combined, the ratio being 1 : 20. The chemically combined CO_2 is chiefly contained in the plasma, only a small amount being in combination in the blood corpuscles. Carbon dioxide splits off the alkalies combined to the blood proteins and combines with the alkalies. This combination of CO_2 with the alkalies, and its subsequent rapid dissociation when the partial pressure of the CO_2 is reduced (*e.g.*, in the lungs), are greatly facilitated by an enzyme **carbonic anhydrase** found in the red corpuscles.

The hæmoglobin assists in the transport of the CO_2 in two ways. Some of the CO_2 may enter the amino groups of the Hb molecule to form carbamino compounds (-NHCOOH). Also, in the red corpuscles HbO_2 acts as a weak acid and combines with potassium to form a compound which may be represented as $KHbO_2$. Carbonic acid from tissue metabolism enters the corpuscles, and the following double decomposition occurs:

$$H_2CO_3 + KHbO_2 \rightarrow KHCO_3 + HHb + O_2.$$

In the plasma there is present NaCl; this is dissociated into Na. and Cl′ ions. The K· ions cannot pass out of the corpuscles, whereas the HCO_3' ions do, and their place is taken by an equivalent amount of Cl′ from the plasma. The net result of this is that KCl appears in the corpuscles, and $NaHCO_3$ in the plasma. This is known as the **Hamburger phenomenon** or the **chloride shift.**

The above process is continuous in the tissue capillaries, while in those of the lungs a reverse action is taking place in the venous blood. The $NaHCO_3$ and the KCl are dissociated. The Cl′

leaves the corpuscles to reunite with the Na + to form NaCl; the CO_2 escapes into the alveolar air; the OH′ recombines with the HHb forming Hb and H_2O. The Hb is now free to reunite with the K to form KHb. It will be seen that the blood, which is now arterial, is rid of the excess CO_2 and ready for another phase of the Chloride Shift.

THE PRESSURE OF THE GASES IN THE BLOOD.— From what has been said, it is clear that we can

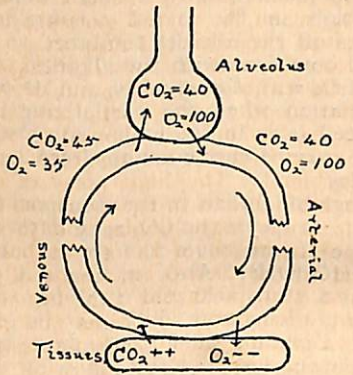


FIG. 21.—DIAGRAM SHOWING PULMONARY AND TISSUE CAPILLARIES, AND THE MOVEMENTS OF GASES TO AND FROM THE BLOOD AS THE RESULT OF DIFFERENCES IN PRESSURE.

The approximate pressures are given in mm. Hg.

consider each gas in the blood as existing under a definite pressure. To take the N_2, for example, the pressure is the same as that of the N_2 in the alveolar air; and as it is not made use of by the tissues, its pressure will be the same throughout the circulation.

The pressure of any gas in a sample of blood is determined by exposing separate portions of the sample individually to different pressures of the gas

in question. By this method one can determine the gas pressure with which the gas in the blood is in equilibrium. The instrument used for this purpose is known as an **aerotonometer.**

From the foregoing it can be concluded that the passage of O_2 from the outside air to the blood, and of the CO_2 from the blood to the lung alveoli, is simply a physical process of diffusion. These gases in each case pass from a place of greater to one of lesser pressure. The contention that the epithelium of the lung alveoli may act as a secreting membrane in regard to O_2, when its partial pressure is very low, has not received experimental support.

RESPIRATORY CHANGES IN THE TISSUES.—The blood itself is not the seat of very active oxidative processes. When arterial blood is drawn, the oxygen in it only slowly disappears when it is allowed to stand. It is in the capillaries that the arterial blood is converted into venous blood. The high pressure of the CO_2 in living tissues helps to bring about the dissociation of the O_2 from oxyhæmoglobin, and so enables the tissues to get as much of the O_2 as possible. The O_2 is carried to the tissues by means of the lymph, and this also transports the CO_2 from the tissues to the blood. Ferments (oxidases and peroxidases) play a part in making the O_2 assimilable (p. 150).

CHAPTER IX

THE DIGESTIVE TRACT—AND ITS GLANDS GENERAL MECHANISM

DIGESTION.

THE food undergoes a process of preparation in the alimentary canal, by which it is rendered **soluble** and **assimilable**—that is, capable of being absorbed. This process is termed digestion. Whether the substance to be digested is protein, carbohydrate, or fat, the changes produced are brought about by **hydrolysis.**

The large molecules are split up into smaller molecules by the introduction of the constituents of water, and this **hydrolytic cleavage** is continued until the molecules are sufficiently small to be assimilated. This process is enormously accelerated by the enzymes contained in the secretions of the alimentary canal and its associated glands. Before these actions can be effectively carried out, certain **mechanical processes** are necessary, by which the food is reduced to a pulp and carried through the alimentary canal. Digestion may therefore be considered under its mechanical and chemical aspects. To understand these it is necessary to have a knowledge of the structure of the alimentary canal with its glands, and of their mode of function.

The Digestive Apparatus.

The digestive apparatus consists of the **alimentary canal,** and the various **glands** which pour their secretions into it. The alimentary canal consists of the mouth, pharynx, œsophagus, stomach, small and large intestines. Numerous glands are situated in the walls of this tract, and the **salivary glands, pancreas,** and **liver** pour their secretions into it.

The Mouth is lined by **mucous membrane,** consisting of a connective-tissue corium covered by stratified squamous epithelium. Numerous small mucous glands occur under the mucous membrane.

The Tongue.—The substance of this organ is chiefly composed of muscle fibres running in various directions. The surface of the mucous membrane is covered with **papillæ,** which are small and simple on the under surface of the organ, and large upon its dorsum, where they are of three kinds: conical, fungiform, and circumvallate.

The **conical papillæ** cover the dorsum of the organ; some are **filiform,** and are elongated by an extraordinary development of the epithelial scales which cover them. In the carnivora the conical papillæ are very largely developed, and give the tongue its characteristic roughness. In man they are probably **tactile organs.**

The **circumvallate papillæ** are from 7 to 12 in number, and are situated at the junction of the middle and posterior thirds of the organ in a **V-shaped line,** with its apex behind. Each is about $\frac{1}{12}$ of an inch in diameter, and is surrounded by an elevated ring **(the vallum),** with a **fossa** between the ring and the papilla.

The **fungiform papillæ** are scattered over the anterior part of the dorsum of the tongue, but are most abundant at its edges. They resemble the circumvallate papillæ, except that their attached portion is constricted (hence their name), and that they are smaller in size. The **circumvallate** and **fungiform papillæ** are gustatory structures and have special organs—taste buds situated on the walls of the fossæ which surround them.

The **taste buds** consist of modified epithelial cells, and are situated in the epithelial layer of the papillæ. They are flask-shaped structures, and consist of a superficial and a central portion. The cells of the superficial portion (**sustentacular cells**) are flat, gradually tapering to either extremity. They are arranged in several layers, and are adherent to each other by their edges so as to form a minute flask. The central portion consists of fusiform **gustatory cells** terminating in hair-like processes, which project from the neck of the flask through an opening—the gustatory pore—formed by the surrounding epithelium. Their deeper extremities are also prolonged, and are branched and varicose. Taste buds are not limited to the mucous membrane of the tongue, but occur also in the soft palate and on the posterior surface of the epiglottis.

THE TEETH.—A **tooth** consists of two parts, one which projects from the gums—**the crown**; the other which is embedded in the socket or alveolus—**the root.** This consists of one or more **fangs.** The constricted portion where these join is called the neck.

The main portion of the tooth is formed of ivory—**dentine**—which is covered in the crown by **enamel** and in the root by a layer of bone—**crusta petrosa.** It is hollow, and contains the **pulp,** which consists of

connective tissue with bloodvessels and nerves and special cells—**odontoblasts.**

Dentine, or ivory, resembles bone in its chemical composition, but contains rather less organic matter. Its matrix is perforated by a vast number of minute branching canals, which extend in a radiating manner from the pulp cavity to the surface of the tooth. These canals are the **dentine tubules,** and they contain processes from the **odontoblasts** which line the pulp cavity, by which the dentine receives nourishment.

Although actual nerve fibres have not been traced into the dentine, it is well known that the superficial surface of the dentine (as when the enamel gets chipped off) is extremely sensitive.

Enamel consists of minute **hexagonal prisms** arranged vertically to the surface of the tooth. It is exceedingly hard, and in the adult contains only about 2 per cent. of organic matter.

The **crusta petrosa,** also called **cement,** is really a layer of bone with rather large irregular lacunæ and canaliculi, and with but few Haversian canals.

Development of the Teeth.—As early as the second month, in the human embryo, the first rudiments of the milk-teeth make their appearance in the following manner. The deeper portion of the epithelium of the mucous membrane becomes thickened, causing a depression of the deep layers of the mucous membrane in the dental region, so that a groove is formed, the **primitive dental groove,** filled with **epithelium,** which becomes the **enamel organ.** This groove becomes transversely divided up into a number of **pouches,** one for each milk-tooth. **Vascular papillæ** of the deep layers of the mucous membrane then grow up, each one being capped with a piece of enamel organ. The enamel organ undergoes differentiation into three layers: an outer layer which lines the tooth capsule, now entirely covered in by the surrounding mucous membrane; a middle layer of stellate cells, forming a spongy tissue; and an inner layer of columnar cells—the **enamel cells.**

At the same time the papilla becomes converted into a layer of cells immediately beneath the enamel organ, odontoblasts, and a spongy vascular tissue—the **pulp.** Calcification then commences at the junction of the enamel cells and the odontoblasts; the enamel is developed outwards in the enamel cells, and the dentine inwards at the expense of the odontoblasts. The stellate cells of the enamel organ gradually dwindle away as the crown of the tooth grows in thickness, until at length the enamel reaches the outer epithelial layer of the enamel organ, which then covers

the crown of the tooth—**Nasmyth's membrane.** The dentine extends beyond the enamel cap to form the root of the tooth, and becomes invested with the crusta petrosa, which is developed from a periosteal membrane, lining the alveolus of the jaw.

The epithelial plug from which the enamel organ is developed gives off a process which penetrates behind the germ of the temporary tooth, and forms a secondary plug beneath it, from which its permanent successor is developed. This remains a germ until the period of the second dentition, when it undergoes the same changes for the development of the permanent tooth that the primary enamel germ does for that of the milk-tooth. The permanent molars, which have no temporary predecessors, are developed from the rudimentary enamel organ of the last milk-molar in the following manner. After the formation of the enamel germ of the second bicuspid, a process of epithelium grows backward from it to form the enamel germ of the first permanent molar, from which the enamel germ of the second molar is derived; this in its turn gives off an enamel germ for the posterior molar. The temporary teeth erupt in sequence from the sixth to the twenty-fourth *month* of post-natal life; the permanent teeth appear from the sixth to the twenty-fourth *year*.

THE SALIVARY GLANDS.—The **saliva** is secreted by three pairs of salivary glands: the **parotid,** the **submaxillary,** and the **sublingual.** These are **racemose** glands, consisting of lobules and lobes bound together by connective tissue enclosing numerous bloodvessels and ducts.

The name racemose is given to such glands because of their resemblance to a bunch of grapes; the secreting parts (**acini** or **alveoli**) correspond to the grapes, the **ducts** correspond to the stalks. Each gland, forming a somewhat bulky structure, is stowed away in a convenient recess near the mouth; the saliva in each case is conveyed by one or many main ducts to the mouth cavity. To collect the secretion for experimental purposes it suffices to insert a cannula into one of these ducts. *The arrangement of the glands in the stomach and in the intestine is different from this, and more elaborate procedures are necessary to collect the secretion from these.*

The **ducts** of the salivary glands are lined by **columnar** cells. The acini are lined internally by secretory epithelium set upon a basement membrane, which in turn is supported by areolar and plain muscle tissue, and surrounded by a close capillary network.

The secreting cells found in salivary glands are of two distinct types; some secrete a thick viscid substance (mucin), others a thin clear fluid; the alveoli are usually filled with one or other kind of cell, and are spoken of as **mucous** and **serous** alveoli respectively. The parotid gland contains only serous alveoli; the submaxillary and sublingual contain both mucous and serous alveoli, and are known as mixed glands.

The cells in the **mucous alveoli** are of two kinds: large cells which almost fill the lumen, and which in

FIG. 22.—SECTION OF THE SUBMAXILLARY GLAND.
c.G., 'Crescents' of Gianuzzi; *m.c.*, mucous cells; *d.*, duct.

stained specimens appear clear, but in the fresh condition are full of **mucigen** granules; between these mucous cells and the basement membrane an incomplete layer of flatter cells is found, which have a somewhat crescentic form when seen in section. These are called **crescents of Gianuzzi,** or **demilune cells**; they are granular even in stained preparations, and secrete a serous fluid, being provided with special **secretory canaliculi,** which pass between the mucous cells to the centre of the alveolus. It will be seen,

therefore, that so-called mucous alveoli are really mixed alveoli; further, that in some parts of the mucous salivary glands the secreting epithelium is two cells deep. (Compare the arrangement in the glands of the fundus of the stomach.)

The cells of the serous alveoli, which in the living condition are full of granules, tend to stain more deeply than the mucus-secreting cells. The ducts of the serous glands likewise stain deeply, and in a section stand out prominently.

Both serous and mucous cells show definite histological changes after activity. The granules diminish in number, especially in the part of the cell which lies next the lumen. The granules of the serous cells, which are supposed to yield the active ferment (ptyalin) of the saliva, are termed **ptyalinogen** granules; those of the mucous cells, which are transformed into mucin (a lubricant material), are termed **mucigen** granules.

The **nervous mechanism** of salivary secretion has been carefully studied in the submaxillary gland in animals. This gland is supplied by the **chorda tympani** and **sympathetic nerves,** the latter being derived from the plexus round the facial artery.

Stimulation of the peripheral portion of the cut **chorda tympani** causes **vaso-dilatation,** and a large secretion of thin **watery saliva,** not wholly dependent upon the increased blood-supply to the gland. If the gland is laid bare, it is seen to become greatly injected with blood: during stimulation of the chorda tympani even its veins become filled with bright-coloured blood and pulsate like arteries; hence it might be inferred that the increased secretion is due to increased blood-supply. If, however, atropine is injected and the chorda tympani is then stimulated, *no secretion of saliva will occur,* although the bloodvessels will be dilated as before. It follows, therefore, that the chorda tympani contains two sets of fibres—**secretory fibres,** which act directly upon the secreting cells, and **vaso-dilator fibres,** which act directly upon the bloodvessels. The atropine paralyses the secretory fibres. Moreover, it has been shown that the saliva poured out during stimulation of the chorda tympani

nerve is secreted at a higher pressure than the blood-pressure within the gland.

The **sympathetic,** when its cut peripheral end is stimulated, causes **vaso-constriction** and a small secretion of rich **viscid saliva.** The latter effect is often absent; nevertheless, it is known that the sympathetic carries secretory—or rather **trophic**—fibres to the gland, because preliminary stimulation of the sympathetic (followed by stimulation of the chorda tympani) increases the solid constituents of the secreted saliva.

Stimulation of gustatory nerves, either directly or through the mucous membrane of the tongue, gives rise to an increased flow of saliva, and at the same time greatly increases the blood-supply to the gland. This can occur only if the chorda tympani is intact. From these facts it is inferred that the increased secretion is a **reflex** act, the gustatory nerves forming the afferent and the chorda tympani the efferent paths of the reflex arc. The centre for secretion lies in the medulla oblongata. Secretion may likewise be excited by afferent impulses reaching the centre by other routes—*e.g.*, by the optic nerves when the mouth waters at the sight of a lemon. Such involuntary responses, more complicated than mere reflexes, involve psychical processes.

The **parotid** receives secretory and vaso-dilator fibres from the glosso-pharyngeal nerve, via the **nerve of Jacobson,** the sympathetic being, as before, vaso-constrictor and trophic.

The Alimentary Canal from Œsophagus downwards.—From the commencement of the œsophagus to the end of the rectum the alimentary canal is arranged in the form of a tube, consisting of a **mucous coat** inside with a **muscular coat** outside, the two being united by loose connective tissue—the **submucous coat.** The muscular coat throughout consists of an external longitudinal and an internal circular layer of muscle fibres; below the upper third of the œsophagus these fibres are of the non-striated variety. A thin stratum of plain muscle fibres, the **muscularis mucosæ,** occurs in the mucous membrane itself, just where it joins the submucous coat. A large number of bloodvessels,

nerves, and lymphatics ramify in the submucous coat.

THE ŒSOPHAGUS has striated muscle in the upper third of its muscular coat. The mucous membrane, which is lined internally with **stratified epithelium,** is so loosely connected with the muscular coat that, when the tube is at rest, it forms plicated longitudinal folds, which entirely fill its cavity. It is plentifully

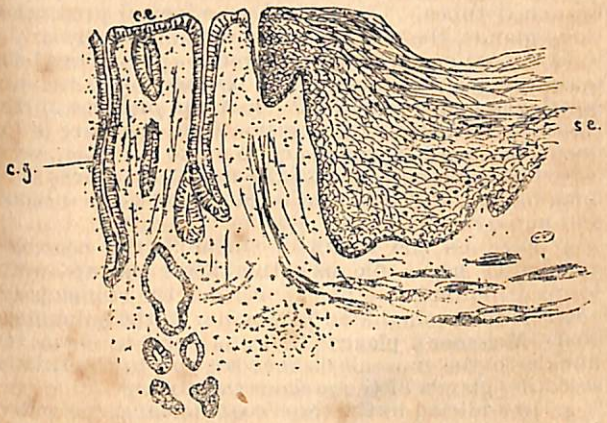


FIG. 23.—SECTION SHOWING THE JUNCTION OF THE ŒSOPHAGEAL AND GASTRIC MUCOUS MEMBRANE.

c.e., Columnar epithelium; *s.e.*, stratified epithelium; *c.g.*, cardiac gland.

supplied with mucous glands, which lie in the submucous coat.

The Alimentary Canal from the Stomach downwards.—In respect to the structure of the digestive tube proper (*i.e.*, the alimentary canal from stomach onwards) certain additional peculiarities of structure fall to be recorded.

1. The lining epithelium of the mucous membrane undergoes an abrupt change in character at the junction of the œsophagus with the stomach. Throughout

the mouth, pharynx, and œsophagus the epithelium is stratified; immediately at the commencement of the stomach it becomes columnar (being one cell deep), which character it retains as far as the anus, where at the junction with the skin the epithelium again becomes stratified.

2. The surface of the mucous membrane of the stomach and intestine is pitted with a vast number of little tubular glands, many of which are simple unbranched tubes. Owing to the universal presence of these glands, the whole mucous membrane forms, as it were, an oozing surface, the secretions poured out being mainly digestive juices. *The thickness of the mucous membrane is due almost entirely to the presence of these glands.* To collect the secretion from any part of this oozing surface it is necessary to make a pocket, say of a part of the stomach or of the intestine, which, while opening to the exterior, still retains its normal blood- and nerve-supply.

3. Between the layers of the muscular coat is a gangliated nerve plexus—**Auerbach's plexus**—which forms a motor nerve mechanism for the stomach and gut. A finer gangliated plexus lies in the submucous coat—**Meissner's plexus**; it sends delicate nerve terminals to the muscularis mucosæ and to the tubular secreting glands of the mucous membrane.

4. In addition to the three coats forming the wall of the œsophagus, a fourth layer, the **serous coat**, is present over the greater part of the digestion tube proper. This coat is external.

The Stomach.—The wall of this organ consists of four coats—serous, muscular, submucous, and mucous. The **muscular coat** is peculiar in that it is composed of three layers—an outer longitudinal, a middle circular, and an internal oblique layer. The middle layer is greatly developed at the pyloric extremity, where it forms a thick ring—the **pyloric valve** or **sphincter**.

The **submucous coat** contains a large number of bloodvessels, nerves, and lymphatics.

The **mucous coat** is connected with the muscular by means of the intervening submucous layer so loosely as to allow of considerable displacement, being thrown

into rugæ in the empty state of the stomach. The surface epithelium consists entirely of mucus-secreting cells (**goblet cells**), which in stained sections resemble the mucus-secreting cells in the alveoli of a mucous salivary gland; they are all, however, columnar in shape.

Dipping down from this surface epithelium into the mucous membrane are the tubular **gastric glands.** Many of these consist of one simple tubule, but usually they branch towards the deeper end. Two, or even three kinds of glands are distinguishable; according to their location they are named—(1) **glands of the fundus**; (2) **glands of the pyloric canal**; and (3) **glands of the cardia,** the last being relatively unimportant, and confined to a narrow zone around the cardiac orifice.

The **glands of the fundus** secrete the precursor of pepsin—**pepsinogen** (and rennin) and hydrochloric acid. The pepsin-forming (**central** or **chief**) cells are arranged side by side in a layer, one cell deep, which lines the interior of the lumen. The acid-forming (**oxyntic** or **parietal**) cells lie external to these, not forming a continuous sheet, but usually isolated from each other; they are provided with special **secretory canaliculi,** which pass between the central cells to the interior of the tubule. As in the case of the mucous alveoli of mucous salivary glands, the secreting epithelium of these glands is thus at places two cells deep. The junction of the glands with the surface epithelium takes place by a narrow mouth.

The **glands of the pyloric canal,** which usually have wide mouths lined by mucous cells, secrete pepsinogen (and rennin), but no acid. Their secretory epithelium consists of a single layer of granular cells. Towards the pylorus they tend to pierce the muscularis mucosæ and to enter the submucous coat, passing by gradual transition into the glands of Brunner of the duodenum.

The **glands of the cardia,** which are partly mucus-secreting, are both simple and compound. Some contain finely granular and some clear and columnar cells.

The **mechanism regulating secretion** of the gastric

glands is largely, though not entirely, nervous. Secretory fibres run down in the **vagus**, stimulation of the peripheral cut end of which excites, after a lengthy latent period, activity of the glands. These efferent secretory fibres are, in the normal economy, excited reflexly by impulses which reach them by other nerve fibres. Simple mechanical stimulation of the gastric

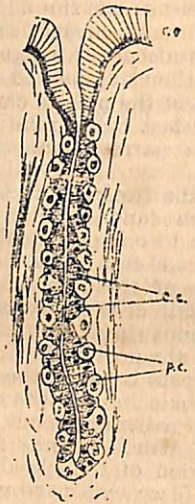


FIG. 24.—SECTION OF A GLAND OF THE FUNDUS OF THE STOMACH.

c.e., Columnar epithelium of the surface; *c.c.*, central cells; *p.c.*, parietal cells.

mucous membrane (mere presence of material in the stomach) does not excite the reflex; on the other hand, the sight or smell of food, the anticipation of a meal by a hungry animal, and, above all, the actual mastication of food, produces, *via* the vagus nerve, abundant secretion. As in the case of salivary secretion, such processes involve psychical action.

These facts have been elicited by experiments on dogs in which the œsophagus had previously been divided in the neck, the disunited ends being separately brought out to the external skin, so that swallowed materials could not reach the stomach, while (artificial) feeding through the lower end was still possible. By this means, too, it has been found that the introduction, without the knowledge of the animal, of certain food materials (especially meat extracts) into the stomach, can, even when both vagi are divided, excite secretion. In this latter case a hormone (**gastrin**), formed by contact of soluble food materials with the pyloric mucous membrane, is probably liberated into the veins of the stomach and carried back with the arterial blood to the fundus region, there exciting the glands. In any case, a mixed extract of pyloric mucous membrane and peptone injected into the blood excites secretion of the fundus glands, whereas either of these constituents injected by itself is without action.

Two processes are therefore involved in the normal stimulation of the gastric glands. The one is a **psychical reflex,** the other involves chemical or **hormone** action. The secretion first poured out is due to the reflex: "hunger is the best sauce." In the absence of this secretion, as from decided loathing or aversion to food, the hormone-excited secretion may, under the action of appropriate foods, still take place.

THE SMALL INTESTINE, which, like the stomach, has four coats, is divided into duodenem, jejunum and ileum. There are, however, no natural divisions, but certain structural characters are more marked in, or are peculiar to, each division (see below), while the transition from one portion to another is perfectly gradual. The **serous** and **submucous coats** in general resemble those of the stomach. The **muscular coat** consists of two layers only—an external layer of longitudinal, and an internal thicker layer of circular, muscle fibre, while between these lies Auerbach's plexus. It is mainly the **mucous coat** of the small intestine that exhibits special and distinctive characters.

As in the stomach, the mucous membrane owes its thickness chiefly to the presence of tubular glands,

here called **crypts of Lieberkühn.** From the free surface of this mucous membrane, however, project an enormous number of fine papillæ or **villi** (see Fig. 29), so thickly set as to confer a velvet-like appearance on the surface. The mucous membrane as a whole is thrown into crescentic folds—**valvulæ conniventes ;** it contains much lymphoid tissue; while the single layer of columnar epithelium lining the surface presents special features.

Valvulæ conniventes.—These are not mere rugæ, but permanent and ineffaceable folds, owing to which

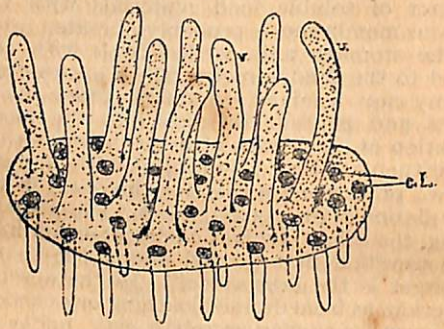


FIG. 25.—PORTION OF THE MUCOUS MEMBRANE OF THE SMALL INTESTINE. (Modified after Rauber.)

c..L, Mouths of crypts of Lieberkühn; *v.* villi.

the surface of the mucous membrane is largely increased. Each fold generally extends from one-half to two-thirds round the intestine. They commence in the duodenum about an inch from the pylorus, where they are but little marked, and they increase in size very rapidly, attaining their greatest development below the opening of the ducts of the liver and pancreas; they extend as far as the middle of the jejunum before they begin to decrease in size, and then gradually diminish until they finally disappear about the middle of the ileum. Some of these folds are $\frac{1}{4}$ of an inch in depth, and are placed so closely that

the spaces between them are scarcely as wide as the valves are thick.

Villi.—Like the valvulæ conniventes, these are peculiar to the small intestine, but are even more characteristic in that they extend from the pylorus to the ileo-cæcal valve, being closely set on every part of the inner surface, over the valvulæ conniventes, as well as between them. Their length is 0·5 mm. or more. Some are cylindrical, some are leaf-like or tongue-shaped. A villus is an outgrowth of the whole mucous membrane, and consists of a central core of reticular tissue, embedded in which are plain muscle fibres, a blood capillary network, and one or more lymphatics (lacteals), and nerve-fibrils from Meissner's plexus. This central core is covered with columnar epithelium, which rests upon a basement-membrane.

The **lacteal** (or lacteals) occupies the centre, and is often somewhat dilated. It serves for the absorption of fats. The **blood capillaries,** lying more peripherally, form a cagework underneath the covering epithelium. By them the carbohydrates and proteins of the food are absorbed. The **muscle fibres,** which lie longitudinally, produce visible retraction of the villus when artificially stimulated. The **columnar epithelium cells** which cover the villus are similar to those lining the general surface of the small intestine, which in turn resembles the epithelium cells of the tubular glands (crypts of Lieberkühn). Seen in profile, they resemble a row of books stacked on a bookshelf; on the free surface each cell presents a vertically **striated border.** Embedded at frequent intervals between these cells are mucus-secreting **goblet cells.** As already indicated, the villi play a highly important part in the absorption of foodstuffs.

The **crypts of Lieberkühn** are simple tubular glands, which open between the villi. Their lining epithelium is similar to that covering the villi, consisting of columnar cells (with striated border) and occasional goblet cells. Sometimes special cells with secretion granules (**cells of Paneth**) occur in the deeper parts of the tubules. These crypts possibly serve in absorption; they furnish the **succus entericus.**

Lymphoid tissue is, for some unexplained reason, specially associated with the mucous membrane of the alimentary tract. It is found in the tongue and pharynx, and somewhat sparsely in the œsophagus, and also to a varying degree in the mucosa of the stomach. In the small intestine, however, and in part of the large intestine, *it forms a conspicuous feature of the mucous membrane.* In the reticular tissue of the small intestine it occurs in the form of densely packed nodules like the cortical nodules of lymphatic glands. Such nodules, when single, are known as **solitary glands;** when aggregated in numbers so as to make a plaque, as **agminated glands,** or **Peyer's patches.** The former occur in all parts of the small intestine. The latter, which are from twenty to thirty in number (more numerous in childhood), are chiefly situated in the lower part of the ileum, being also peculiar in that they are limited to that part of the gut most distant from the mesentery. They are not covered by villi as a rule, and are surrounded by a zone of lymphatics even more abundant than in other parts of the intestinal wall.

Special characters are exhibited by the duodenum and by the ileum. In addition to the crypts of Lieberkühn in the mucous membrane, the **duodenum** possesses in the *submucous coat* compound tubulo-racemose glands, known as **Brunner's glands,** more marked in herbivora than in carnivora, but always present, and absolutely diagnostic of that part of the gut. The **ileum,** as above mentioned, is especially characterised by the presence of **Peyer's patches.**

The secretion of the small intestine seems to be governed by the presence of food in the active part. There are also indications that hormones may have a controlling influence, but the experimental evidence is somewhat conflicting.

The bile of the liver and the pancreatic secretion enter the duodenum. Pancreatic juice contains at least three digestive ferments. On the other hand, bile contains *no ferments,* its action being merely accessory to the enzymes of the pancreas. The main function of the pancreas being to secrete digestive enzymes,

we find that its structure is essentially similar to that of certain digestive glands already described. On the other hand, the formation of an *external* secretion by the liver is secondary in importance to its main

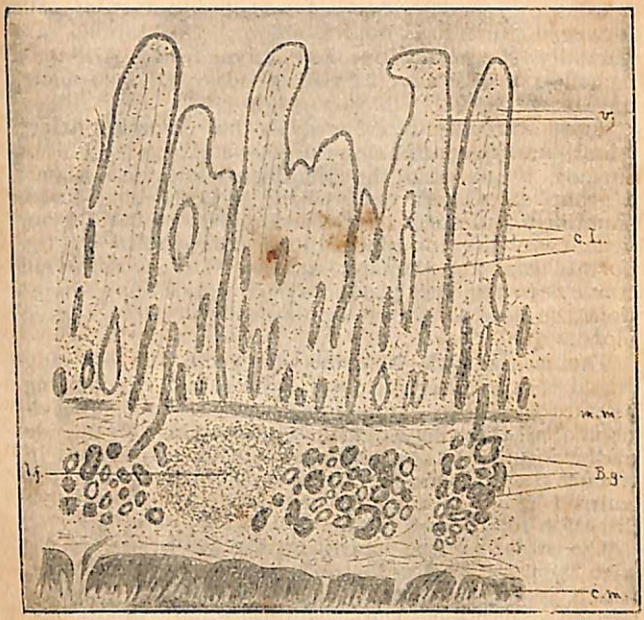


FIG. 26.—SECTION OF DUODENUM.

v, Villi; *c.L.*, crypts of Lieberkühn; *m.m.*, muscularis mucosæ; *B.g.*, Brunner's glands; *l.f.*, lymphatic follicle; *c.m.*, circular muscular layer.

functions, which are to elaborate and partially to store food materials reaching it by the portal vein; its structure is consequently *sui generis*, and is best described in terms of the arrangement of its blood-vessels.

THE LIVER is the largest gland in the body. It weighs about 3 pounds (adult), or one-fortieth of the weight of the body. In an infant it is relatively heavier, forming one-eighteenth of the body weight. It is composed of lobules, which, however, do not consist of secreting alveoli or tubules, but of cells arranged in more solid fashion. The lobules are partially separated by connective tissue (**Glisson's capsule**), in which are carried bloodvessels, bile-ducts, and lymphatics.

Two afferent bloodvessels—the **hepatic artery** (small) and the **portal vein** (large)—enter on its inferior surface, where also the **bile-duct** leaves the gland; a group of efferent vessels—the **hepatic veins**—more superiorly and posteriorly placed, carry to the inferior vena cava the combined blood that enters by the portal vein and hepatic artery. The portal vein conveys to the liver products of digestion for elaboration; the hepatic artery supplies ordinary oxygenated blood.

The issuing bile-duct lies alongside the entering portal vein and hepatic artery, the three vessels being bound together by connective tissue. As the subdivisions of all three continue for a time to lie side by side in the interior of the organ, it will be convenient in tracing them inwards to speak of the bile-duct as if it coursed from without inwards—*i.e.*, in the reverse direction to the flow of bile.

The three vessels, penetrating into the interior, carry with them, as it were, their connective tissue covering, which, partially surrounding each lobule, becomes Glisson's capsule, the main internal supporting framework of the gland. The smaller branches of the entering vessels, in their penultimate subdivision, come to lie *between* the lobules, and are known in consequence as **interlobular** branches.

Each lobule is a mass of liver cells separated by capillary-like bloodvessels, which converge from the periphery of the lobule towards its centre. These vessels take common origin from the interlobular veins and arteries; they converge on a (usually) single, centrally placed vein, which, from its position *within*

the lobule, is called **intralobular.** The intralobular veins are the smallest branches of the *hepatic* veins, towards which they converge by becoming on the route **sublobular** veins. The blood of the intralobular-sublobular-hepatic efferent system is therefore separated from the arterial-venous afferent system simply by the capillary-like vessels that course between the liver cells. It is here that these cells act upon the blood constituents.

The endothelium of the capillary-like vessels is deficient, so that the blood comes into actual contact with the hepatic cells, even penetrating into their interior by means of minute **intracellular blood-channels.** The relation between blood and cells is therefore a most intimate one. Closely applied to the lumen of the capillary-like vessels are found separate cells of a flattened form (**stellate cells of Kupffer**), which are highly phagocytic towards injected carmine grains or towards hæmolysed or foreign erythrocytes. These vessels with defective or absent endothelial lining are not true capillaries, but **sinusoids.** Vessels of this nature, which have a wider and less regularly cylindrical lumen than ordinary capillaries, are more common in developing than in adult animals. They arise by in-pushing of solid columns of cells into larger blood-spaces, not, like capillaries, by ingrowth of blood-channels between masses of cells.

The **hepatic cells,** polyhedral in form, have a round nucleus and granular cytoplasm. They often contain, especially after a meal, fat and glycogen; in conditions of excessive hæmolysis they contain iron-holding pigment granules (**hæmosiderin**), derived from hæmoglobin. In addition to the intracellular blood-channels mentioned above, they have a second system of still finer intracellular canals, which communicate with the bile-ducts.

The **bile-ducts,** which receive the secretion from these latter channels, commence at **intercellular bile canaliculi,** lying *between* adjacent hepatic cells, each cell of an adjacent pair having a groove or gutter which fits against a corresponding groove in its neighbour. These canaliculi form a network which opens at the

periphery of the lobule into the **interlobular bile-ducts.** These latter are lined with columnar epithelium, by which they are readily recognised lying in Glisson's capsule.

It is not known how the liver **lymphatics** take origin. The liver forms a very large amount of lymph. Lymphatic vessels accompany both the portal vein and the portal hepatic veins, the chief outflow of lymph taking place by the first of these two systems. Numerous **nerves** are distributed to the bloodvessels.

It is a remarkable fact that, important as the liver is, in some forms of chronic (*e.g.*, amyloid) disease of the gland the amount of liver-cell tissue may be reduced to a mere fraction of the normal, and yet the patient long continues to live.

The bile issues from the liver by two **hepatic ducts,** one from each lobe. These unite to form the common hepatic duct. In its course towards the duodenum this gives off a diverticulum consisting of the **cystic duct** and **gall-bladder,** the latter of which contains much plain muscle in its wall and is lined by columnar epithelium, which secretes mucus. The **bile-duct** is the name given to that part of the tube which lies next the duodenum. The liver is the only gland of the alimentary canal provided with a storage reservoir.

Mechanism of Secretion.—There are no secretory nerves to the liver. Its secretion, which is continuous, may experimentally be influenced, however, by stimulation or section of the splanchnic nerves, which convey vaso-constrictor impulses to the bloodvessels (the portal vein itself is under the influence of these nerves). Stimulation of the splanchnics reduces and section of the nerves increases the flow of bile. The action of the nervous mechanism is indirect.

Direct stimulation may be produced by chemical agents (cholagogues). Injection or feeding with bile-salts, or injection of secretin (see under Pancreas), gives rise to an increased secretion of bile. For the composition and functions of bile see p. 127 et seq.

Expulsion from the Gall-bladder.—The entrance of acid-containing contents from the stomach into the duodenum brings about a contraction of the muscular

wall of the gall-bladder. Soaps and fats have the same effect. A hormone named **cholecystokinin** has been extracted from the mucosa at the commencement of the jejunum. When injected it causes contraction of the gall-bladder. No doubt the entrance of this hormone into the bloodstream is facilitated by the passage of chyme into the duodenum.

THE PANCREAS.—The structure of this gland is very similar to that of the parotid. The alveoli, however, are more elongated, the connective tissue between the lobules is looser, and the gland contains special collections of epithelial cells (**islets of Langerhans**). The latter have no excretory ducts; they have special sinusoidal capillaries, and *they do not atrophy* like the alveolar cells when the duct of the pancreas is ligatured or otherwise blocked. They yield the *internal* secretion of the pancreas which is concerned in carbohydrate metabolism and to which the name **insulin** has been given.

Mechanism of Secretion.—The *external* secretion is stimulated by a hormone, and also by the vagi. The hormone (**secretin**) is produced by the duodenal mucous membrane when the hydrochloric acid ejected by the stomach through the pylorus comes in contact with it. A hydrochloric acid extract of duodenal mucosa, when neutralised and injected into the blood stream, stimulates secretion of the pancreas (and also of the liver), while a saline extract of duodenal mucous membrane alone is unable under similar circumstances to excite activity of the gland. Secretin is a fairly stable chemical substance; it withstands the temperature of boiling water, and is therefore not a ferment.

Evidence has been adduced which suggests that secretin exists *as such* in the mucosa, and that its entry into the blood stream is facilitated by the presence of bile-salts in the partially neutralised chyme.

It has been shown experimentally that although secretin causes a copious flow of pancreatic juice, the latter is poor in enzymes. When, however, the *vagi* are stimulated, the enzyme content rises.

THE LARGE INTESTINE consists of the **colon,** with the **cæcum** and **vermiform appendix,** and the **rectum.**

It has four coats, like the small intestine, but the cæcum, ascending and descending colons are only partially covered by peritoneum, and the lower portion of the rectum is entirely devoid of any peritoneal covering. The external longitudinal fibres of the muscular coat of the colon and cæcum form three bands, between which the wall of the tube is sacculated.

The **mucous membrane,** which differs from that of the small intestine in being smooth and devoid of villi and valvulæ conniventes, is chiefly composed of **tubular glands,** which are larger than those of the small intestine, and contain a vastly greater number of cells

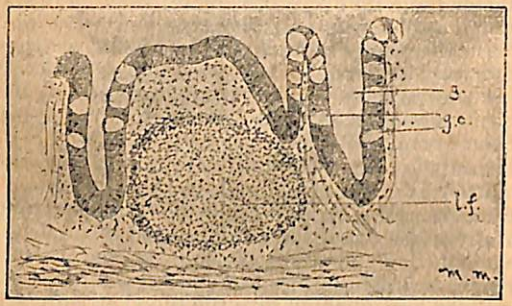


FIG. 27.—SECTION OF LARGE INTESTINE.

g., Gland; *g.c.*, goblet cells; *l.f.*, lymph follicle; *m.m.*, muscularis mucosæ.

charged with **mucin.** The surface epithelium is precisely similar to that of the small intestine. There is a muscularis mucosæ and very numerous **lymphatics,** similar to those of the stomach and small intestine; the arrangement of the bloodvessels is also similar to that between the tubular glands of the small intestine. The **solitary lymphatic nodules** in the mucous membrane are larger and more numerous than in the small intestine.

The **vermiform appendix** projects from the lower end of the cæcum, is invested in peritoneum, and has a mesentery of its own. In structure it resembles the

cæcum and colon, and is especially rich in **lymphoid tissue.**

The **ileo-cæcal valve** is a double transverse fold of mucous membrane which guards the entrance of the small into the large intestine. When the cæcum is distended, its edges are brought into apposition, so that, although it offers no resistance to the passage of substances from the small into the large intestine, it entirely prevents their regurgitation. The surfaces of this valve which look towards the small intestine are covered with **villi,** whilst those towards the cæcum are entirely without them.

The **rectum** is smooth externally, as it is entirely surrounded by an even layer of longitudinal muscular fibres. It has a very thick layer of circular fibres, which are especially developed near its extremity, where they form the **internal sphincter.** Its mucous membrane is very movable on its muscular coat, and is thrown into strongly marked longitudinal folds in the lower portion of the gut, and into transverse folds in its upper part. These are effaced in its distended condition.

The Muscular Movements of Digestion.

The food is subjected to the action of the teeth—mastication—and mixed with saliva in the mouth.

Mastication is effected by the vertical, lateral, and antero-posterior movement of the lower jaw, by which the food is pressed and triturated between the upper and lower teeth. During the process of mastication the food is kept between the teeth by the combined movements of the **tongue** and the **buccinator** muscles, by which it is prevented from accumulating between the teeth and the cheeks. The proper mastication of the food is exceedingly important, as the action of the gastric and intestinal fluids upon it is greatly accelerated by its minute subdivision. This is especially the case with vegetable substances, which are otherwise frequently passed through the whole alimentary canal in an unchanged, or nearly unchanged, condition.

During the mastication the food is mixed with the saliva, so that it may be converted into a mass, or **bolus,** on the dorsum of the tongue, and rendered fit to be swallowed.

Deglutition.—The masticated food is gathered up by the tongue and formed into a bolus between the tongue and hard palate. The tongue is then pressed from before backwards against the roof of the mouth, and the bolus slips back, through the fauces, and is ultimately grasped by the pharyngeal muscles, and passed into the œsophagus. The act of deglutition is divided, for convenience of description, into three stages.

The **first stage** is a voluntary act, by which the food is carried back to the anterior pillars of the fauces.

The **second stage** of the act of deglutition consists in the passage of the bolus from the anterior pillars of the fauces to the commencement of the œsophagus; this is a **reflex act,** and is **performed very rapidly,** as the food has to pass over the opening of the larynx. As soon as the bolus arrives at the isthmus of the fauces, the pharynx is prepared for its reception. The hyoid bone is drawn forwards and upwards so that the larynx is protected by the base of the tongue, which projects over it, the glottis being closed at the same time, and the vocal cords approximated so as to close the rima glottidis. It should be noted that the **epiglottis** does not fold like a lid over the opening of the glottis, but stands erect throughout. The pharynx itself is shortened and drawn forward by the contraction of the palato-pharyngei muscles, which approximate towards each other like a pair of side-curtains; the soft palate is also raised and made tense, thus cutting off the upper part of the pharynx and posterior nares, and forming an incline under which the bolus is passed into the pharynx. This passage is effected by the elevation of the hyoid bone and the base of the tongue, and the simultaneous contraction of the pillars of the fauces. The most important muscles concerned, however, are the **mylo-hyoids.** The bolus is then seized and carried rapidly down past the larynx by the pharyngeal con-

strictors. During the second stage of deglutition **respiration is reflexly inhibited.**

The *afferent* nerves regulating deglutition are the branches of the fifth nerve in the palate and of the glosso-pharyngeal nerve in the pharynx. The *motor* nerves are branches of the fifth, supplying the muscles of mastication, and branches of the spinal accessory, glosso-pharyngeal and hypoglossal. Liquids are swallowed by the same mechanism, and, in the absence of food, the second part of the act of deglutition can be performed only when its nervous mechanism is incited to activity by the passage of saliva through the fauces.

The **third stage** of the act of deglutition involves the passage of the food through the **œsophagus.** The rate at which the food is carried along this tube depends on its consistency. Liquids are shot down from the upper to the lower part in a small fraction of a second; a bolus of solid food is forced along in more leisurely fashion by peristaltic movement of the musculature, the total time of transmission being about six seconds. The peristaltic movement is controlled at every point by impulses arriving through the vagus nerve, and is not a wave propagated by mere muscular conduction; the propagation of the movement is **reflex.** On the arrival of the peristaltic wave at the cardiac orifice of the stomach, the circular muscle in this region relaxes its tonic contraction, and the food passes into the stomach. Liquids, which have been rapidly shot down, are not allowed to enter the stomach until the peristaltic wave originally excited by the act of swallowing has in its leisurely course arrived at the cardiac orifice. From this we infer that the opening of the cardiac orifice is part of the reflex.

The Movements of the Stomach.—Solid food remains in the stomach for some hours; liquid food is rapidly passed into the duodenum. The fundic part of the stomach has little or no active movement, serving merely as a reservoir to contain a meal until the more active pyloric region has by peristaltic contraction churned up and intimately mingled with the gastric secretions successive portions of the mass contained

in the fundus, meanwhile delivering these portions at intervals into the duodenum. The fundus merely exercises a steady pressure on the food; the pyloric part arranges for its transport in successive fractions towards the small intestine.

These facts have been determined by feeding an animal with food containing bismuth carbonate, which casts a dark shadow when the stomach is examined with Röntgen rays. The appended figures show the gradual change in form and size of the fundus as the food becomes digested; the pyloric part is meantime involved in successive onward travelling waves of contraction. The pyloric sphincter, unlike the cardiac orifice, does not relax on the arrival of each peristaltic wave. It continues closed for long periods, and opens at irregular intervals, possibly when the food is sufficiently liquid. Direct injection of acid into the duodenum serves to keep the sphincter closed, and it may be that the orifice relaxes only after each gush of acid chyme has been neutralised. It will be noted that no churning or intermingling of different portions of the food takes place in the fundus.

While the stomach receives nerves from two separate sources, vagus and splanchnic, its movement is not dependent on the integrity of these nerves; in other words, it is more or less **automatic.** The excised stomach kept in a bath of warm oxygenated saline undergoes rhythmic movements. Stimulation of the vagus nerves, however, serves to increase the normal movements; the **vagus** is therefore **motor.** Stimulation of the **splanchnics** (sympathetics) diminishes or annuls the movement: these nerves are **inhibitory.**

Movements of the Small Intestine.—Like those of the stomach, the movements of the intestines are automatic—that is, independent of central nervous control. They are of two kinds, **peristaltic** and **segmental** (pendular). The peristaltic movement, like that of the œsophagus, drives the food onwards, at a slow rate however. The pendular movements are best seen when the abdomen of an animal is opened under warm saline solution. Under these conditions a given loop of gut may swing from side to

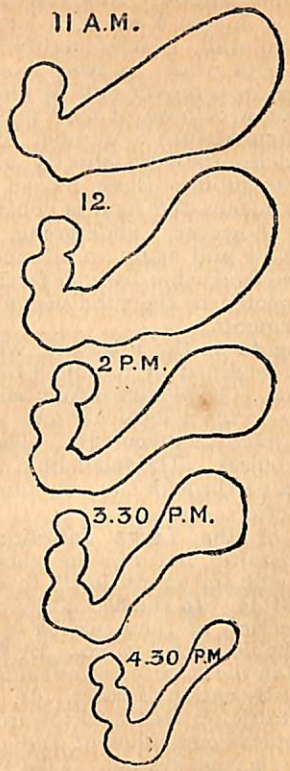


FIG. 28.—OUTLINES OF A CAT'S STOMACH SEEN BY RÖNTGEN RAYS AT VARYING PERIODS AFTER A MEAL (AFTER CANNON).

The outlines of the stomach, containing food mixed with bismuth carbonate, were drawn.

I., Immediately after a meal; II., one hour later; III., three hours later; IV., four and a half hours later; V., five and a half hours later.

side in a rhythmic fashion. Analysis of this movement shows that it is due to a series of local constrictions of the intestinal wall, which, modifying its rigidity, cause the gut as a whole to sway from side to side. Study of the pendular movements by means of Röntgen rays shows that a column of food in the intestine is suddenly **segmented** into a number of short blocks. A new constriction-pattern shortly afterwards subdivides and recombines these blocks in a different way. By this means the food is constantly churned up, without, however, undergoing any forward movement. Now and again an advancing peristaltic wave carries the food some distance farther, whereupon it is again subjected to the subdivision process of the pendular movements.

The movements of the intestine, while essentially automatic, are modified by impulses from the central nervous system. The plexus of Auerbach between the muscular coats forms a local nervous mechanism for at least the peristaltic movements. The **vagus** nerves carry **motor** impulses. The **splanchnic** nerves reaching the small intestine through the semilunar plexus have an **inhibitory** action.

Movements of the Large Intestine.—These are chiefly of peristaltic nature, the successive waves being less frequent and more slowly travelling than in the small intestine. In the ascending and transverse colons the direction of these waves is for the most part towards the ileo-cæcal valve. By this means the food is retained in the large intestine sufficiently long to allow of a large absorption of water. In the descending colon the peristaltic waves travel towards the rectum.

These movements are inherent and not originated by the central nervous system. Like the rest of the gut, however, the large intestine receives motor and inhibitory fibres. The latter are derived from the splanchnic nerves. The former, instead of being derived from the brain by means of the vagus, come from the sacral region of the cord, and are distributed by the *nervi erigentes*. It should be noted that the *inhibitory* outflow to the smooth muscle of the *whole gut* is derived as *sympathetic nerves* from the middle

region of the spinal cord. The *motor* fibres are either cranial or sacral, according to level.

Defæcation.—Whereas the musculature of the middle part of the alimentary canal is largely independent of the central nervous system, this is not the case at the oral and rectal extremities. Like the process of swallowing, defæcation is a complicated reflex action, and in the infant is unassociated with any voluntary control. A certain amount of voluntary control, chiefly inhibitory, is developed at a later stage. Two sphincter muscles, kept in constant tonic action, guard the exit of the rectum. The internal sphincter is a strong band of the circular coat of the gut, and consists of involuntary muscle. The external sphincter, to a certain extent under the control of the will, is composed of striated muscle. Defæcation is partly voluntary, partly involuntary. The purely reflex element of the act consists in contractions of the strong musculature of the rectum with relaxation of the sphincter muscles. The voluntary element consists in the inhibition of the external sphincter and in contraction of the abdominal muscles and diaphragm. The essentially reflex nature of the process is brought out by the fact that in an animal with complete transection of the spinal cord in the lower dorsal region, defæcation is performed normally. The spinal section for the reflex lies in the lumbar cord, disease or destruction of which produces long-continued relaxation of the sphincters, with involuntary escape of fæces.

Vomiting is also a complicated reflex, over which there is little or no voluntary control. It is usually preceded by a sensation of nausea with reflex flow of saliva into the mouth. Retching movements follow, in which spasmodic inspirations are made with glottis closed, the negative pressure in the thorax, including the thoracic part of the œsophagus, being thereby much increased. Next, owing to convulsive contraction of the abdominal muscles, the contents of the stomach are ejected through the inhibited cardiac sphincter. As the food passes the glottis, this opening is reflexly closed.

A vomiting centre exists in the medulla oblongata. It can be directly stimulated by the drug apomorphine. Usually, however, it is excited by afferent stimuli arriving by various sensory nerves, especially from the stomach itself by way of the vagus. The efferent paths are the motor nerves which innervate the muscles concerned, vagus, phrenics, and spinal nerves to the abdominal muscles. The vomiting centre is in close relation to the respiratory centre. Indeed, vomiting involves simultaneous action of expiratory muscles (abdominal) and inspiratory muscles (diaphragm).

CHAPTER X

DIGESTION AND ABSORPTION

Foodstuffs undergo in the body chemical changes which may for practical purposes be classified under three headings: (1) Hydrolysis; (2) deamination; (3) oxidation and reduction. In hydrolysis the large molecule takes up water and then splits into smaller parts. Deamination, which concerns only protein foods, comes into play especially in the liver. Oxidation causes a giving up of energy, and takes place chiefly in the tissues themselves. Ferments or enzymes play an important part in bringing about these changes, and this is particularly demonstrable in the process of digestion. Consequently, before proceeding to the study of digestion, it is necessary to say a few words concerning the general mode of action of enzymes.

Enzymes.

Enzymes may be looked upon as being **organic catalysts;** they act solely by facilitating the rapidity of a reaction, but they themselves are not used up in the process. They are formed in the cells of living organisms, and their chemical composition is unknown.

Practically all the enzymes found in the body are concerned in hastening hydrolytic cleavage (**hydro-**

lysis), and this is true whether the substances acted upon be proteins, carbohydrates or fats. Certain properties are common to all the enzymes.

They are all *thermolabile*, most of them being destroyed when heated to 80° C. In every case *water* must be present and either the enzyme or the substrate, or both, must be in solution. All enzymes have an optimum *temperature* at which they function. That of the body enzymes is about 40° C. Each has an optimum *H-ion concentration* in which it functions; some, for instance, are effective in an acid medium and are destroyed by alkalies, others are the reverse.

All enzymes must have a **co-enzyme** to facilitate their activities, and this co-enzyme is usually an inorganic substance—*e.g.*, pepsin and HCl. All enzymes are *specific* in their action, the substances upon which they act being known as **substrates.**

Some act only on carbohydrates, others on proteins, and others again on fats. They are specific, however, even in a more strict sense than this, for some enzymes will act only on certain substances of a group, and will not act on even closely related substances of the same group. This specificity forms a convenient basis upon which to classify the enzymes. The following are a few examples. Proteases (proteolytic enzymes) split up proteins—*e.g.*, pepsin, trypsin; amylases (amylolytic enzymes) act on starches—*e.g.*, ptyalin; lipases (lipolytic enzymes) hydrolyse fats—*e.g.*, lipase, steapsin.

Only small quantities of an enzyme are necessary to act on even large amounts of the substrate. The reaction probably takes place in two stages: (1) combination between enzyme and substrate, and (2) in splitting up of the resulting product with formation of the end-products of the reaction. This process is in many cases reversible, and to obtain the full value from an enzyme the products of its hydrolytic activity should be removed as soon as they are formed.

It must be clearly understood that enzymes *do not initiate* the action It is their function to hasten to an enormous extent a process which would otherwise take a very long time to occur. For example, if a

solution of starch is allowed to stand, a few weeks will elapse before hydrolysis will have proceeded far. If a similar solution is boiled, hydrolysis will occur in several hours, but if a small amount of acid is added the time will be reduced to a few minutes. If, however, to such a solution of starch there is added an amylase, hydrolysis will take place in a few seconds.

In some cases the enzyme which the cell produces is inactive; this inactive form is known as a **zymogen** or **pro-enzyme,** and it requires a second substance to activate the enzyme. Such an activating substance is known as a **kinase** if it is an organic substance, or an **activator** if an inorganic substance. The best example is the enterokinase of the intestine, which, acting on trypsinogen, forms the active trypsin.

When enzymes are injected into an animal, substances are produced in the serum of that animal which oppose the action of the injected enzymes. The tissues of the body seem to protect themselves against the action of enzymes by the production of specific anti-enzymes. It will be noted, therefore, that enzymes resemble toxins, both in the way they act upon other substances, and in the reaction they call forth when injected into the bodies of animals.

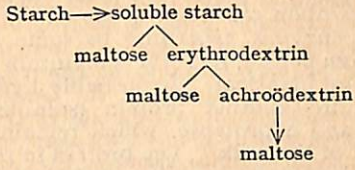
Besides the enzymes that are found in the various secretions, known as secretory- or exo-enzymes, there are also enzymes known as **intracellular** or **endo-enzymes,** which help to carry out the metabolism in the cells that form them, and on the death of the cells they may bring about a self-digestion or **autolysis** of the protoplasm of the cells in which they are formed.

Digestion.

In the Mouth.—The glands of the mouth produce **saliva.** This is a colourless, turbid, and viscid fluid, slightly alkaline, and having a specific gravity of about 1·005. It consists mainly of water containing about 0·6 per cent. of solids—mucin, albumin, an amylolytic enzyme (**ptyalin**), and inorganic salts. The chief salts in the saliva are sodium chloride, sodium phosphate.

calcium bicarbonate, and traces of potassium thiocyanate.

Saliva has a physical and a chemical function. Its physical action is to moisten the food and thus to help deglutition. The chemical action of saliva is limited to the conversion of starch into dextrin and maltose, and is due to the presence of the ptyalin which acts only in slightly alkaline or in neutral media. The action of ptyalin on the starch may be shown as follows:



Usually the food stays too short a time in the mouth for these changes to take place, but the ferment goes on acting in the stomach so long as no free acid is present. Ptyalin does not act readily on raw starch owing to the cellulose which envelops the starch granules.

In the Stomach.—Gastric juice obtained from the stomach of a fasting animal is a clear fluid, and contains about 0·5 per cent. hydrochloric acid. Owing to admixture with the food this acidity is soon reduced to 0·2 per cent. HCl, and remains at this level during digestion.

The activity of the juice depends upon the hydrochloric acid and **pepsin.** This enzyme, which is secreted in an inactive form (pepsinogen) by the central cells of the fundus and from the glands of the pylorus, requires the presence of hydrochloric acid to activate it. It hydrolyses proteins, splitting them up into peptones. The action of the gastric juice on proteins depends upon a number of conditions: (1) As a rule animal proteins are more easily digested than those of vegetable origin. (2) Too much acid or too little acid retards the rate of change; each kind of protein requires its own optimum concentration of acid. (3) In alkaline solution the enzyme is *destroyed,* while bile suspends its activity. (4) As the end-products—

proteoses and **peptones**—accumulate, the action is suspended.

The activity of any sample of gastric juice may be measured by Mett's method. Short lengths of narrow glass tube filled with coagulated egg-white are left for varying periods in the fluid to be tested. The rate at which the enzyme eats into the egg-white is measured. This in turn gives the activity of the sample of gastric juice.

Gastric juice contains also another enzyme—**rennin**—which acts upon caseinogen, one of the proteins of milk. This enzyme, according to some authorities, is distinct from pepsin, but others maintain that rennin and pepsin are identical. It probably hydrolyses the caseinogen into another protein (soluble casein or paracasein) and a proteose, which remains dissolved in the serum of the milk. The protein in the presence of calcium salts forms a complex combination, **insoluble casein,** which is precipitated, and so leaves a fluid known as the whey. This precipitate is acted upon by the gastric juice, and a part of it is dissolved. Casein is utilised in the manufacture of cheese.

Carbohydrates are not appreciably affected by gastric juice (the hydrochloric acid, however, may act upon cane-sugar, inverting it to glucose and fructose). Fats and oils are not acted upon by gastric juice. By digesting the protoplasmic envelopes of the fat globules of adipose tissue, the gastric secretion aids in setting the fat free.

In addition to the effect on proteins the gastric juice is also of importance in sterilising the food and drink by killing pathogenic bacteria. This antiseptic quality of the gastric juice is due to the hydrochloric acid.

In the Intestine.—The chyme, or chemically altered food, from the stomach comes under the influence of three sets of secretions, derived from the pancreas, the liver, and the tubular glands of the intestine.

Pancreatic Juice is a clear, opalescent fluid, alkaline in reaction because of the presence of sodium bicarbonate. It contains proteins, chlorides, and at least three enzymes, which act respectively on proteins, carbohydrates, and fats.

The proteolytic enzyme (**trypsin**) is not active when obtained directly from the pancreatic duct; only when it comes in contact with the succus entericus is it activated by a material known as **enterokinase.** Calcium salts are also known to have the power of activating trypsinogen.

Trypsin acts best in a slightly alkaline or in a neutral medium, a strongly alkaline or an acid medium destroying its *action.* It is more powerful than pepsin. It splits proteins and the products of peptic digestion into the simpler abiuret products, such as polypeptides and **amino-acids.** The latter products are rapidly absorbed, and their presence in the small intestine cannot be easily demonstrated. Tryptic digestion of certain proteins takes place more readily after they have been submitted to the influence of the gastric juice—*e.g.*, serum is not readily acted upon by trypsin alone; but if it has been first acted upon by pepsin and hydrochloric acid, then the trypsin can readily split it up.

The diastatic enzyme of pancreatic juice (**amylopsin** or **amylase**) has the power of converting starch in exactly the same way as ptyalin.

The lipolytic or fat-splitting enzyme (**lipase**) splits neutral fats into glycerol and fatty acids. In an alkaline medium these fatty acids combine with the alkali and form soaps. The lipolytic action of lipase is augmented by adding bile. The bile salts (1) lessen the surface tension between the water and oil, and (2) help to dissolve soaps as well as fatty acids. On absorption by the epithelial cells of the intestine, the bile salts are separated from the fatty acids, the latter being resynthetised into neutral fats, whilst the bile salts are carried by the portal system to the liver, and are resecreted with the bile.

Bile is an alkaline fluid, of a golden-brown, red, or greenish colour, having a specific gravity of 1·010 to 1·050. Its composition varies according as to whether it is taken directly from the bile-ducts or from the gall-bladder. In the gall-bladder the bile becomes thicker, partly owing to the absorption of a considerable amount of water, partly owing to the fact that

a new constituent—mucin—is added to it. The important constituents in the bile are the bile salts, bile pigments, cholesterol and lecithin.

There are two **bile salts**—namely, glycocholate and taurocholate of soda. When glycocholic and taurocholic acids are hydrolysed (by heating with acids or with alkalies), they both yield a substance known as cholic or cholalic acid (nitrogen-free and related to cholesterol). In glycocholic acid this substance is combined with the amino-acid, glycine; in taurocholic acid it is combined with taurin, a sulphur-containing amino-acid.

Bile salts owe their great importance to the part they play in aiding the digestion and absorption of fats.

Bile salts are detected by Pettenkofer's test, which depends upon the presence of cholalic acid. A small amount of cane-sugar is added to the bile, and the two shaken together. When sulphuric acid is now added, a purple colour is produced. The sulphuric acid acts on the cane-sugar, forming furfurol, which in turn combines with cholic acid to produce the purple substance.

The bile pigments are likewise two in number—namely, bilirubin (red), and an oxidation product thereof, biliverdin (green). They are derived entirely from the hæmoglobin of the blood. The constant excretion of bile pigments indicates a continuous breaking down of red blood corpuscles. When hæmolytic agents are added to the blood, an increased amount of bile pigment is excreted.

While these pigments have no important physiological function, they impart a dark colour to the fæces, the absence of which in jaundice (due to some obstruction of the bile-duct) is an important clinical sign. The actual pigments present in the fæces are derivatives (stercobilinogen and stercobilin) from bilirubin. Much of the bile pigment does not pass out with the fæces, but is reabsorbed to be excreted again by the liver. Of this moiety a small portion may be excreted in the urine as urobilinogen.

Bile pigments are detected by Gmelin's test, which

consists in the addition of fuming nitric acid. This acts as a strong oxidising agent, and forms variously coloured oxidation products, so that a play of colours is produced in the following order—green, blue, violet, red, yellow.

Cholesterol, a non-nitrogenous crystalline substance forming rhombic plates with a notched angle, is a monohydric secondary alcohol, insoluble in water or in cold alcohol. Its presence in the bile, in which it is held in solution by the bile acids, can be shown by extracting the bile with ether, and dissolving in some chloroform the residue left after evaporating the ether, and then shaking up with an equal part of strong sulphuric acid. The chloroform on separating is seen to be coloured red, whilst the sulphuric acid, which is yellow, shows a fluorescence.

Amongst other substances found in bile are lecithin, fats, soaps, and traces of urea. Besides calcium and magnesium phosphate, iron is also present, but is *not a constituent of the bile pigment.* It is generally combined with phosphoric acid.

The gall-bladder sometimes contains biliary concretions, or gall-stones. These vary in size, form, and number. Three varieties are met with: (1) Cholesterol stones are the commonest, and have a low specific gravity; a varying amount of pigments may also be present. (2) Pigment calculi, which consist mainly of bilirubin combined with calcium, biliverdin also being sometimes present. (3) Stones composed mainly of inorganic substances, such as carbonate and phosphate of calcium. These last are very rare in the human gall-bladder.

Bile may be looked upon partly as an *excretion,* because of the contained bile pigments, which are disintegration products of the red blood corpuscles, and partly as a *secretion,* because of the bile salts which help in the process of digestion. The formation of bile is continuous, but it is discharged into the gut only as required; otherwise, it is temporarily stored in the gall-bladder.

Occlusion of the bile-duct by ligation or by any pathological changes—*e.g.*, presence of a gall-stone—

causes the bile to get into the blood, producing jaundice or **icterus,** so called because of the characteristic yellow colour produced in the skin. The fæces are pale, and bile is present in the urine. In spite of the obstruction in the main duct, the hepatic cells go on forming bile, which is absorbed by the lymphatics and so reaches the blood.

Succus Entericus, or intestinal juice, has an alkaline reaction due to the presence of sodium bicarbonate. Specimens of it may be obtained by making a Thiry-Vella fistula in the small intestine. This consists in taking an isolated portion of the gut still attached to its mesentery, and stitching it to the abdominal wall so that the two ends open to the outside of the body. Five enzymes have been demonstrated in the succus entericus.

Three of these act on disaccharides: cane-sugar is inverted into dextrose and lævulose by **invertase;** milk-sugar, or lactose, is split into dextrose and galactose by the ferment **lactase;** maltose is split into two molecules of dextrose by **maltase,** which is subsidiary to and completes the action of ptyalin and amylopsin. It is seen, therefore, that ingested carbohydrates are all eventually converted into mono-saccharides.

Erepsin is an important proteolytic ferment. It cannot attack native proteins, and acts upon these substances only when they have been previously hydrolysed to proteoses or to peptones. This proteolytic ferment completes the action of pepsin and (to a less extent) of trypsin on proteins. Erepsin forms the same end-products as trypsin.

Reference has already been made to the substance **enterokinase,** the so-called "ferment of ferments," which converts trypsinogen into trypsin.

Besides the various juices which take part in intestinal digestion, the intestine also contains a large number of bacteria. These bacteria excite putrefactive and fermentative processes, and are responsible for the presence of gases in the gut. In the small intestine only those bacteria which cause fermentation of carbohydrates are active, and the organic acids—lactic, acetic, etc.—thus produced have an inhibitory action

THE CHIEF ENZYMES TAKING PART IN DIGESTION.

Enzyme.	*Where found.*	*Site of Action.*	*Reaction of Medium.*	*Substances acted upon.*	*Products.*
Ptyalin ..	Saliva	Mouth and stomach	Slightly alkaline or neutral	Starch	Dextrins and maltose
Pepsin ..	Gastric juice	Stomach	Acid	Proteins	Proteoses and peptones
Rennin ..	" "	"	"	Caseinogen	Casein
Trypsin ..	Pancreatic juice	Small intestine	Alkaline or neutral	Proteins	Polypeptides and amino-acids
Amylopsin (amylase) ..	" "	" "	" "	Starch	Maltose
Steapsin (lipase) ..	" "	" "	" "	Fats	Glycerol and fatty acids
Erepsin ..	Succus entericus	" "	" "	Proteoses and peptones	Amino-acids
Maltase ..	" "	" "	" "	Maltose	Glucose
Invertase (sucrase) ..	" "	" "	" "	Cane-sugar or saccharose	Glucose and fructose
Lactase ..	" "	" "	" "	Milk-sugar or lactose	Glucose and galactose
Enterokinase ..	" "	" "	" "	Trypsinogen	Trypsin

on the putrefactive changes produced by other bacteria on proteins, while they neutralise the alkaline secretions of the gut. The contents of the small intestine have a neutral reaction.

Absorption.

Absorption means the taking up of the products of digestion from the alimentary tract into the lymph and blood stream, and includes any chemical changes that may occur in the process.

There is no evidence to show that absorption of any consequence occurs in the **stomach.**

The **Small Intestine** plays the most important part in absorption. Its surface is greatly increased by the numerous villi. Each villus has two channels by which it carries off the products of digestion that have passed through the surface epithelium: (1) the **central lacteal,** communicating with the subjacent intermuscular lymph plexus; (2) the **capillary bloodvessels** which collect the blood into veins joining the mesenteric branches of the portal vein. The lymph plexus is supplied with valves, which aid the onward flow of the fluid.

The absorption of hypotonic solutions as well as of dissolved substances may take place by a process of diffusion or osmosis. The vital action of the cells, however, also comes into play, as is shown by their high selective power. Thus a hypertonic solution of sodium chloride can be absorbed by the cells and passed into the blood, despite its lower osmotic pressure. Other sodium salts—*e.g.*, the sulphates—are not readily absorbed, and may increase the peristalsis of the gut. A selective power is also shown in connection with the heavy metals, of which only iron is absorbed. Again, if an animal's own serum is introduced into the intestine, complete absorption takes place although the osmotic tension may be the same on both sides of the mucosa.

Fats.—In order to be absorbed fats must be completely digested into fatty acids and glycerol. The lipase which splits the fat is assisted in its action by the alkaline juices poured into the gut. As soon

as any fatty acid is formed on the surface of a fat-droplet, it combines with alkali to form a soap. The surface-tension over the droplet is now reduced, and it breaks into smaller droplets. Owing to the larger surface thus formed, the lipase acts more rapidly on the remainder. By the combined action of the lipase and the alkali, the whole droplet becomes first mechanically broken up, and eventually disintegrated into its chemical constituents. The bile-salts likewise assist absorption by reducing the surface tension of the bowel contents.

The glycerol and fatty acid in a state of solution enter the epithelial cells, where they combine to form fat once more. This fact can readily be shown by histological methods—*e.g.*, staining with osmic acid. The free or striated border of the epithelial cells is clear; below this fine fat-droplets are present, while further towards the fixed end of the cells these droplets increase in size. The synthesis is produced by lipase, which is reversible in its action. The fat is mechanically conveyed from the epithelial cells to the central lacteal of the villus. Sixty per cent. of the absorbed fat can be collected from the thoracic duct. Evidence is accumulating to show that the glycerol and the fatty acids may be absorbed uncombined via the capillaries of the villi into the portal circulation.

Extirpation of the pancreas causes almost all the fat to appear in the fæces (absence of lipase). With a biliary fistula (absence of bile-salts) the absorption of fats is reduced.

Carbohydrates are absorbed chiefly as monosaccharides, through the capillaries of the villi. Disaccharides, if present in high concentration, may be absorbed to a slight extent, but are not retained in the body.

Proteins are absorbed in various stages of decomposition, but especially as dipeptides and amino-acids. They, also, enter through the bloodvessels of the villi.

Excretion by the Intestine.

Fæces consist partly of the indigestible residue of the food (cellulose, etc.), partly of true excretory products.

The contents of the small intestine are fluid and not offensive. In the large intestine, by the absorption of water, the contents become semi-solid; owing to bacterial action, with the production of materials like skatol, indol, etc., the material acquires an offensive odour. In the large intestine little absorption of food materials occurs, but excretion of minerals—*e.g.*, calcium, phosphorus, magnesium, and iron—takes place. There is a considerable secretion of mucus, which acts as a lubricant, and many disintegrated epithelial cells are added to the fæces. Curiously enough, most of the bacteria that pass out with the excreta are found to be dead.

With vegetable diet the excreta are more voluminous than with animal diet. On a mixed diet the amount of fæces is usually about one-seventh of the food ingested. Their consistency is little dependent upon the amount of water drunk. Their reaction is practically neutral in cases where the diet is mixed; starchy food, owing to the formation of lactic acid, gives an acid reaction; a meat diet, owing to the production of ammonia, gives an alkaline reaction. The bile is not entirely responsible for the colour of the fæces, although biliary pigments are present.

CHAPTER XI

METABOLISM AND ANIMAL HEAT

THE term 'metabolism' includes all the chemical changes undergone in the body by the food and by the absorbed oxygen. The oxygen is taken in by the lungs, the food by the alimentary canal, and the metabolised end-products are excreted principally by the lungs and by the kidneys. These effete products are found to have undergone oxidation, the carbon and hydrogen having been completely oxidised to carbon dioxide and water, any sulphur or phosphorus to sulphate or phosphate, the nitrogen alone escaping from the body in an incompletely oxidised state.

Metabolism of Absorbed Foodstuffs.

In Chapter X. there was described the mechanism by which the constituents of the diet were digested and finally absorbed. It now remains to discuss the ultimate fate within the body of these absorbed products. The food is composed of three proximate principles—proteins, carbohydrates, and fats. The proteins are taken *primarily* to repair and build the body tissues, and if not required for this purpose, they are got rid of immediately. This is accomplished by altering their structure and then burning them. The carbohydrates and fats are taken *primarily* to provide energy, and when not so used they are *stored in the tissues*. Therein lies an essential difference between these two subdivisions of the food.

Proteins.—These are absorbed as *amino-acids*, the units by which the body is to build up its own characteristic proteins. Ordinarily more amino-acids, both quantitatively and qualitatively, are absorbed than are required. They are carried by the portal circulation to the liver. Most of the unwanted amino-acids go no further, the remainder pass out by the hepatic vein and are circulated throughout the body. The various tissues withdraw from the blood such amino-acids as they require, and eventually all the unwanted acids are again returned to the liver. These acids, along with those not circulated to the tissues, are not stored, but in their present form the body cannot oxidise them. This is due to the presence in their molecule of the amino group (NH_2). Accordingly, in order to render them combustible, they are **deaminised.** This consists in removing the elements of ammonia from the molecule, leaving behind a *keto-acid*. This may be shown in the case of the amino-acid, **alanine**:

$$CH_3CHNH_2COOH + O \longrightarrow CH_3COCOOH + NH_3$$

The keto-acid thus created (in this case pyruvic acid) is very readily combustible, and provides a potent source of energy. Indeed, these keto-acids are more easily oxidised than carbohydrates, and because of the very readily available energy obtained from the

' unwanted ' amino-acids, this has been referred to as the **specific dynamic action** of the proteins. It may be noted that the liver is not the only organ which possesses the power to deaminise. The muscles also have this property.

This ammonia which is set free is not harmless to the tissues, and if allowed to accumulate in the blood, toxic conditions, if not actually death, would ensue. This is, however, prevented by further changes. Carbonic acid is present in all the tissues of the body, and the ammonia combines with this to form ammonium carbonate. *In the liver* this compound has two molecules of water removed from it, and is thus converted into **urea.** The process may be represented as follows:

$$\underset{\text{(Ammonium carbonate)}}{(NH_4)_2CO_3} \text{ minus } H_2O = \underset{\text{(Ammonium carbamate)}}{(NH_2)(NH_4)CO_2}$$

$$\underset{\text{(Ammonium carbamate)}}{(NH_2)(NH_4)CO_2} \text{ minus } H_2O = \underset{\text{(Urea)}}{(NH_2)_2CO}$$

The changes outlined above are based upon the assumption that urea has the carbamide structure there shown. Evidence, however, has been produced to show that urea has a cyclic formula, and the suggestion has been made that it is derived in the body from **cyanic acid** (HOCN). In the tissue fluids this is readily hydrolysed to ammonia and CO_2. The ammonia thus liberated combines with the more stable *keto* form of cyanic acid (HNCO) to form urea, with the cyclic formula:

For the formation of urea from arginine, see *appendix.* **Urea** is innocuous to the tissues, and after leaving the liver it is eventually carried to the kidneys, where it is excreted in the urine. *The urea output from the body varies directly with the protein intake.*

Besides urea, other decomposition products of pro-

teins appear in the urine, among the most important of which are ammonia, phosphates, and sulphates. Some of the ammonia which is split off from the amino-acids may combine with acids other than H_2CO_3, in which event it is excreted in the urine. Any unusual production of acids in the body will therefore increase the ammonia output with a corresponding reduction in the urea output. This is seen particularly in *starvation*, and in *diabetes mellitus* (*q.v.*), in which conditions appreciable amounts of hydroxy-acids may be produced in the body. The phosphates and the sulphates are derived from the P and S respectively which were combined in the protein molecule. Other protein excretory products are referred to in the chapter on urine.

In **starvation** the total amount of nitrogen excreted gradually diminishes during the first three days, after which it remains fairly constant. This lasts as long as the energy requirements are supplied from the fat depots of the body. When the fat is used up the total nitrogen excretion rises, owing to the protein of the body being now used for energy purposes. This latter state of affairs soon brings about the death of the animal.

Nucleoproteins.—These proteins are so called because they are found mainly in the nuclei of cells. They are therefore found in greatest concentration in cellular organs, such as kidney, liver, and pancreas. They are frequently referred to as **purine compounds,** because of the presence in all of them of substances containing the purine ring.

Nucleoproteins are combinations of nuclein and protein, and the former is a combination of *nucleic acid* with protein. The digestion, absorption, and metabolism of the protein fractions follow the usual course for proteins, but the nucleic acid requires special comment.

Nucleic acids are complex compounds differing according to their source. They are all formed by the combination of four *nucleotides*, and each of the latter is derived from the combination of H_3PO_4 with a *nucleoside*.

The **nucleosides** are composed of a carbohydrate combined with a *purine* or a *pyrimidine* base. The purine bases are **adenine** and **guanine**; the pyrimidine bases are cytosine, uracil, or thymine. Thus:

Carbohydrate + purine (or pyrimidine) = nucleoside.
Nucleoside + H_3PO_4 = nucleotide.
4 × nucleotides = nucleic acid.

The nucleic acid is acted upon in the small intestine by an enzyme (*polynucleotidase*), and the mono-nucleotides set free. Those containing purines are acted upon by *nucleotidase*, and their components liberated. This is shown as follows:

Nucleic acid → nucleotides → (H_3PO_4 / nucleosides (purine bases) / nucleosides (pyrimidine)) → { carbohydrates, adenine, guanine }

The adenine and guanine are acted upon by specific enzymes and oxidised to **uric acid.** In the case of man and the higher apes, oxidation stops at this stage. In all other mammals it is carried a stage further to form **allantoin.** The metabolism of the H_3PO_4 and the carbohydrates calls for no special comment.

The nucleoproteins metabolised in the body are partly of *endogenous* and partly of *exogenous* origin. The end product, uric acid, is excreted as such in the urine, either free or combined as urates. When no nucleoproteins are given in the food, the excretion of uric acid is fairly constant in amount, but it may be increased in fevers or after excessive muscular activity.

Carbohydrates.—Carbohydrates are taken primarily to *supply energy*. The amount absorbed after a meal is usually much in excess of the immediate requirements of the body. They enter the portal circulation in the form of monosaccharides, and are carried to the liver. From here some of the glucose passes by way of the hepatic vein into the general circulation, and the sugar content of the blood slowly rises. The degree of this rise is determined by the balance between the glucose leaving the liver and the extent to which the tissues are utilising it. Some of the glucose

is retained by the liver, and stored in the liver cells in the form of **glycogen.** This change is brought about by an enzyme, *glycogenase.* The enzyme can not only build up glycogen, but it can also hydrolyse it to form glucose again. This occurs when the glucose in the circulating blood falls below a certain level, and this hydrolysis is hastened by the secretion of *adrenaline* into the bloodstream. Not only the liver, but also the *muscles,* can synthesise and store glycogen.

When these storehouses become full, and the intake of carbohydrate continues in excess of the energy requirements of the body, the sugar is then converted into **fat,** and stored as such.

By these means the sugar content of the blood is kept between 0·08 and 0·12 per cent. Should it rise above 0·18 per cent., the condition is called **hyperglycæmia,** and the excess sugar is now excreted by the kidneys. The appearance of easily detectable amounts of glucose in the urine is known as **glycosuria.**

Hyperglycæmia can be produced by (1) injecting intravenously small quantities of sugars, such as cane-sugar, lactose, or glucose; (2) giving very large amounts of sugar *per os*; (3) injection of adrenaline; (4) injection of pituitrin; (5) 'diabetic puncture' (Claude Bernard), in which the floor of the fourth ventricle is punctured; and (6) removal of the pancreas (pancreatic diabetes), with the consequent absence of its internal secretion (insulin), which plays an important part in carbohydrate metabolism. Another experimental form of glycosuria, in which, however, there is *no hyperglycæmia,* is that obtained after the injection of phlorhizin (a glucoside). This drug impairs the absorptive function of the kidney tubules, as a result of which sugar is excreted. In man a disease occurs, known as *diabetes mellitus,* in which large quantities of glucose are excreted with the urine, and the amount of water excreted per diem is also increased. This condition is accompanied by a hyperglycæmia and by the presence of acetone bodies in the blood and urine (**ketosis**); it is very often fatal, especially in young people. The injection of 'insulin (p. 113)

diminishes the hyperglycæmia and ketosis, and greatly improves the condition of the patient.

Fats.—The fats differ from the amino-acids and the monosaccharides in their channel of absorption. After being resynthesised in the epithelium of the villi, they pass into the central lacteal. The exceedingly small particles of fat may be lying free in the lymph, or they may be found ingested in the lymphocytes. The fat is conveyed into the lacteals of the mesentery, and by way of the *cisternum chyli* and the thoracic duct, it eventually reaches the blood stream (*see also p.* 133). If not required for immediate oxidation it is laid down in the various fat depots, to be oxidised as required. The body is peculiarly averse to storing 'foreign fats,' those characteristic to each animal being manufactured from the excess carbohydrate intake. Fats, however, are readily oxidised, and provide a valuable source of energy.

When required for oxidation the fats are hydrolysed by the tissue lipase. The glycerol is oxidised, and the fatty acids are transported to the liver, where they are *desaturated*. This consists in the oxidation of two H atoms, one from each of two adjacent C atoms in the fatty acid chain. The large molecule is now split into fatty acids of smaller size. Thereafter the two terminal carbons in these molecules, with their attached hydrogen atoms, are oxidised to CO_2 and H_2O, leaving a smaller fatty acid. This process (known as β oxidation) is repeated, *two carbons* going off at a time, until acetic acid is reached, which is finally oxidised to CO_2 and H_2O.

Up to the stage of butyric acid ($CH_3CH_2CH_2COOH$) no difficulty is encountered. The next step, that of oxidising the butyric acid into two molecules of acetic acid, cannot take place *unless the carbohydrate metabolism is proceeding normally*. Thus, in conditions such as starvation or diabetes mellitus, the β carbon is only partially oxidised, yielding β-hydroxybutyric acid ($CH_3CHOHCH_2COOH$). The next step in this faulty fatty metabolism is the production of aceto-acetic (diacetic) acid (CH_3COCH_2COOH), which is readily changed into acetone (CH_3COCH_3). These

end products appear in the expired air and in the urine, and the condition is known as **ketosis.** Because of the appearance of these unwanted acids in the blood, the term *acidosis* has frequently been employed. The use of this word, implying as it does an acid condition of the blood, is misleading: *the blood is never acid.*

Determination of Body Requirements.

The amount of food metabolised depends upon the actual requirements of the body, be it for the repair and growth of the tissues or for the output of energy, and *not upon the amount of food ingested.* It is a relatively simple matter to measure and examine the amount of food and oxygen taken in by the body, and to collect and examine all the end-products. To trace the successive steps by which the one group is transformed into the other in the body is, however, a very difficult task, and frequently we have to be content simply to compare the intaken food with the excreted end-products.

For the examination of the intaken food it is not sufficient merely to reckon the quantity; an analysis of the substances composing the food must also be made. It must be known how much carbohydrate, how much fat, and how much protein is present. In the last case it is necessary only to estimate the amount of nitrogen; this multiplied by 6·25 gives approximately the amount of protein which it represents. Even then, to know how much of this food is actually absorbed by the body, the unutilised food that appears in the fæces must be deducted. Similarly the oxygen intake can be arrived at by subtracting the oxygen expired from the oxygen inspired into the lungs.

As already indicated, the only excretory products derived from carbohydrates or from fats are carbon dioxide and water. The end-products derived from protein foods are mainly nitrogen-containing substances (urea, ammonia, creatinine, etc.), and small quantities of sulphates and phosphates, all of which

appear in the urine. If the total nitrogen in the urine is estimated the amount of protein metabolised can be determined.

When the nitrogen-intake of a person balances his output, he is said to be in **nitrogenous equilibrium.** Nitrogen is retained in the body only when required for the building up and repairing of tissues, and is

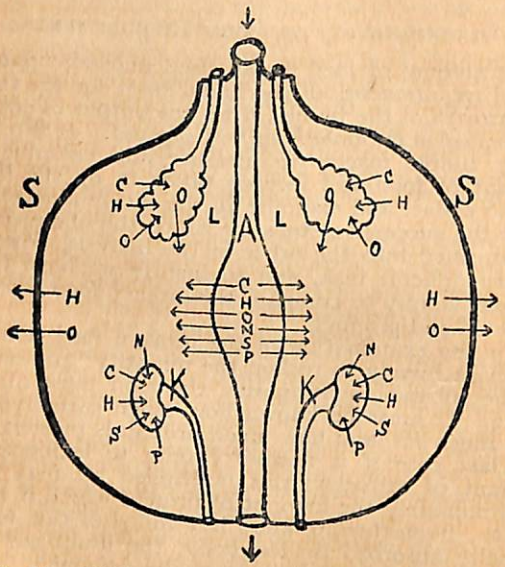


FIG. 29.—DIAGRAM OF ABSORPTION AND EXCRETION OF ORGANIC SUBSTANCES (MODIFIED FROM STEWART).

A, Alimentary canal; *L*, lungs; *K*, kidney; *S*, skin; *C*, carbon; *H*, hydrogen; *O*, oxygen; *N*, nitrogen; *P*, phosphorus; *S*, sulphur.

not otherwise stored. In wasting diseases, on the other hand, the amount of nitrogen excreted is greater than the amount of nitrogen taken in as food.

By means of the foregoing methods, and by deter-

mination of the intake as well as of the output, it is seen whether there is a retention of food material, or a balance, or a greater output of substance than is taken in. It is necessary to know, too, what use is made of the food materials by the cells of the body—*i.e.*, whether the foods are used mainly to replace loss due to tear and wear of the tissues, or whether they are used to supply energy (work or heat). The food requirements of the body for energy purposes *always exceed those for tissue repair.*

Metabolism and Tissue Waste.—Living protoplasm is constantly undergoing changes, consisting in a breaking down of the protoplasm (catabolism), which can only be counterbalanced by fresh material being taken in (assimilation) and synthetically built up into new protoplasm (anabolism). Besides these ordinary changes in the cells, certain special substances are formed (secretions, etc.). Secretions may be reabsorbed in part, but much of them is lost. The food-material derived from actual living cells is known as **endogenous,** in contradistinction to the food-material which comes from without, and which is known as **exogenous.** In the case of proteins, this endogenous origin of nutriment is well known, a good example being seen in the case of the salmon, which develops its reproductive organs at the expense of the skeletal muscles. Similarly in starvation it is found that certain tissues, which are not so important to the organism, undergo atrophy first in order to supply the other more important organs (such as the heart and brain) with food-material.

One of the most important problems in chemical physiology is to determine how much protein is just necessary to repair the loss due to tear and wear. The protein minimum cannot be determined by means of a starvation experiment because of the fact that protein can also be utilised for the supply of energy, and in starvation a part of the protein is thus utilised. If, however, the energy requirements of the body are supplied by a sufficiency of carbohydrates and fats, all protein being withheld in the food, it is possible approximately to estimate the amount of protein

catabolised by determining the quantity of nitrogen excreted in the urine. Experimental investigations have shown that for a person of 70 kilos doing a moderate amount of work the daily excretion of nitrogen is from 4 to 7 g. This represents a breakdown of 25 to 44 g. of protein which must be replaced each twenty-four hours. To assure a sufficiency of *essential* amino acids, two to three times this weight of protein should be eaten.

Energy Value of Foods.—The cells of the body are constantly at work. Even during bodily rest some of the muscles are actively working (heart, diaphragm), and certain cells are forming secretions (bile, hormones), or excretions (urine). The amount of work done during rest is constant for the same individual, provided the pre-experimental and the external conditions are constant, but it varies with the size, age and sex of the subject. Now, the cells of the body require food to supply them with the necessary energy —the energy arising from **oxidation** of the food. In the case of carbohydrates and fats this oxidation is complete, but in the case of proteins it is not complete, since they are partly excreted as urea. It would seem therefore that provided the food can be oxidised, and so supply energy, its composition does not matter. Carbohydrates can theoretically be replaced by isodynamic quantities of fats or of proteins. It must however be noted, that although certain substances may be able to give the same amount of energy, they may not be so amenable to oxidation in the body—carbohydrates, for example, oxidising more readily than fats. It is possible to estimate the total energy of the food-materials in terms of heat. The unit used is the calorie, which is the amount of heat required to raise 1 gramme of water through 1° C. A large Calorie (spelt with a capital C) is the amount of heat required to raise 1 *litre* of water through 1° C., and is therefore equal to 1,000 small calories.

To estimate the caloric value of a food substance a known quantity of the dried material is completely burnt in a closed vessel surrounded with water; the rise of temperature of the water, multiplied by its

weight, gives the quantity of heat given out in the process. The average caloric values for the chief food substances are:

Carbohydrates	(1 gramme) ..	4·1	Calories
Proteins*	.. do. ..	4·1	,,
Fats	do. ..	9·3	,,

Energy Requirements of Body.—In order to apply the above information, the next step is to determine the energy requirements of the body. This may be done by measuring the amount of O_2 consumed by the body, the amount of CO_2 given out by the lungs, and the quantity of N_2 excreted in the urine. From the last figure, the amount of protein metabolised can be found, and with this knowledge it is easy to calculate from the first two figures how much fat and carbohydrate respectively has been oxidised. This is done by reference to the respiratory quotient.

The **respiratory quotient** (R.Q.) is the ratio of the amount of CO_2 expired to the amount of oxygen absorbed from the inspired air. This ratio depends upon the kind of food being oxidised. A typical carbohydrate such as glucose has the formula $C_6H_{12}O_6$. To oxidise completely such a molecule only six molecules of oxygen (O_2) are required, because the oxygen already present is sufficient to oxidise the hydrogen. We thus see that in carbohydrate oxidation the intake of oxygen (in volume) is balanced by an equal output in volume of carbon dioxide, and this ratio, which is known as the respiratory quotient, will, in the case of a person who is utilising only carbohydrates, be $\frac{CO_2}{O_2}=1$. Fats and proteins do not have all their hydrogen atoms satisfied with oxygen, and in these cases more oxygen will be required than is necessary to oxidise the carbon. This extra oxygen leaves the body combined as water. When, therefore, a person utilises proteins or fats only, the oxygen intake will

* This is the physiological caloric value of proteins. They are not completely oxidised, part being excreted as urea. The true value for proteins is 5·7 Calories.

exceed the output of *carbon dioxide*, and so the respiratory quotient will be less than 1. Where only fat food is oxidised it is about 0·7; where only protein food is oxidised, about 0·8.

When, therefore, the proportions of the foodstuffs being burned in the body are found, and the total oxygen utilised has been measured, the calorie output can be readily *calculated*. As a rough approximation it may be stated that each litre of oxygen utilised in the body represents an output of 5 Calories.

Experimental observations have shown that the energy requirements of the body depend mainly upon the *surface area*. In the male adult these *average* 40 Calories per square metre of body surface per hour, under basal conditions. This is known as the **basal metabolic rate,** and is obtained with the subject lying down and at rest, at least fourteen hours after the last meal was taken. A person standing up expends about 10 per cent., and when walking about 30 per cent., more energy than when lying down.

Children require more calories per *kilo of body-weight* than do adults. This is because they possess a *relatively* large surface from which they lose heat.

The Calorie requirements of an individual may be calculated as follows. The surface area of an adult male may be taken as 1·8 square metres. Multiplying this by 40, there is obtained the Calorie output per hour at rest, amounting to 72 Calories. Assuming that an individual spent eight hours sleeping, eight hours working, and eight hours at leisure, then the calculation would be as follows:

Sleep	8 × 72 =	576 Calories
Work (treble the basal rate)	8 × 216 =	1,728 ,,
Leisure (1½ times basal rate)	8 × 108 =	864 ,,
Total		3,168 ,,

These figures represent the Calorie requirements of a normal adult performing moderate work. An individual leading a sedentary life would require about 2,100 Calories. A person undertaking hard work would require from 4,000 to 4,500 Calories.

It has been found that if the Calorie requirements of a man have been determined, those for a boy of fifteen years or for an adult woman would approximate to 85 per cent. of this amount. For a girl of fifteen years 75 per cent. would be required, and for a four-year-old child, 36 per cent.

Requirements of a Diet.—In constructing a diet certain fundamentals should be observed. The food should be sufficient in amount, of the correct quality, and such as to appeal to the palate. Tissue building and repair require proteins; energy is best supplied by carbohydrates and fats. In addition to these **proximate principles** there must be a sufficiency of inorganic salts, water, and vitamins. In the adult about 40 g. of proteins have to be replaced every twenty-four hours. In order to assure, however, that the body is able to obtain the particular amino-acids which it requires for rebuilding purposes, the protein intake should be greater than 40 g., and the proteins should be varied in nature. Experience has shown that an intake of 100 g. of mixed proteins fulfils these requirements. The energy derived from these proteins will be $100 \times 4{\cdot}1 = 410$ Calories. The remainder of the Calorie requirements are now made up with fats and carbohydrates. There are differences of opinion as to the proportions in which the latter should be present, but a ratio of 1 to 4 or thereby proves satisfactory.

On this basis a diet for an individual doing moderate work, as shown above, would be as follows:

Proteins	100 g. × 4·1 =	410 Calories
Fats	100 g. × 9·3 =	930 ,,
Carbohydrates ..	450 g. × 4·1 =	1,845 ,,
Total		3,185 ,,

One might expect that there would be an increase in the protein metabolism during muscular work, owing to increased catabolism of muscle-protoplasm. Actually, however, an increased output of nitrogen does not occur unless an insufficient amount of carbohydrates and fats is taken. Moreover, when the

respiratory quotient is examined, it is found to be unaffected by work. This points to the fact that none of the three principal foodstuffs is used in preference to others.

The quality of the proteins in the diet is of importance. The amino-acids of which the different proteins are composed are not of equal value to the body for growth purposes. It has been demonstrated that proteins of vegetable origin are apt to lack 'essential building units.' This also applies to the animal protein, gelatin. Further, the diet may be sufficient to maintain life, but fail to bring about growth. The criteria of a satisfactory diet are that it should be able to maintain the body weight and mental and physical efficiency, and it should assure nitrogenous equilibrium.

For long it was considered that proteins, carbohydrates and fats, together with inorganic salts and water, were alone necessary to maintain growth and health. The discovery of 'vitamins,' however, altered this view.

Vitamins.

The vitamins, which are sometimes termed 'accessory food factors,' are active in very small quantities, and the presence of most of them in the diet is essential if health, and sometimes life, is to be maintained. When their presence was first demonstrated in foodstuffs, and for a long time afterwards, their chemical nature was unknown. It was found convenient, therefore, to label them after the letters of the alphabet. As their function became known there was a tendency to name them with reference to their properties—*e.g.*, anti-rachitic, pellagra-preventing. The chemical composition of most of them has now been determined, but as their formulæ are generally very complicated they are still frequently referred to by the letters A, B, C, etc. The more important properties of the vitamins are briefly outlined below.

Vitamin A is manufactured by the animal from its precursor *carotene*, which is found in green plants. Three forms of carotene are known, α, β and γ, but

the β carotene has double the vitamin A activity of either the other two. One molecule of the *beta* carotene, $C_{40}H_{56}$, plus one molecule of H_2O, yields two molecules of vitamin A, $C_{20}H_{29}OH$.

Vitamin B complex consists of several components, designated B_1, B_2, etc. $\mathbf{B_1}$ is a heat-labile, water-soluble solid *thiamin chloride*, with the empirical formula $C_{12}H_{17}N_4SOCl.HCl$; it is also known as **aneurin.** It is necessary for the proper functioning of the nervous system and is intimately concerned in carbohydrate metabolism. With pyrophosphoric acid it forms an ester which acts as a co-enzyme to carboxylase. Without these, pyruvic acid cannot be oxidised and so accumulates in the tissues, which then lose their power to respire. This results in damage to the nervous system, kidneys and heart. Gross deficiency of B_1 leads to the condition known as beri-beri.

$\mathbf{B_2}$ has been subdivided into two fractions—(*a*) a *growth-promoting* and (*b*) a *pellagra-preventing* factor. The former is a heat-stabile, water-soluble substance known as **riboflavin,** and has the empirical formula $C_{17}H_{20}N_4O_6$. This substance is essential for growth. It is the pigment present in the "yellow enzyme" of Warburg and Christian, found in cells all over the body, and acting as a carrier of oxygen in cell respiration. The second fraction in B_2 is known as the **P-P factor,** and is an oxidation product of nicotine—*nicotinic acid* (C_5H_4NCOOH). Its amide has been isolated from the liver, and both this and the acid have been used successfully in the treatment of pellagra in man, black tongue in dogs, and dermatitis in the pig.

Vitamin C was the first vitamin to be allotted a definite structural formula, and it was the first to be synthesised. It is also known as **ascorbic acid** on account of its power to prevent scurvy. The empirical formula is $C_6H_8O_6$. It is found in citrus fruits, tomatoes, turnips, etc., and in great concentration in the cortex of the adrenal glands. In addition to its antiscorbutic properties this vitamin is also believed to be necessary for the maturation of the red blood corpuscles.

Vitamin D.—Under this general term are included a number of closely related vitamins, two of which, D_2 and D_3, are discussed here. Both of these can be produced by the action of sunlight or ultra-violet rays upon certain sterols. **D_2, also known as calciferol,** may be obtained by the irradiation of *ergosterol*, a sterol found in ergot and other plant sources. Calciferol is not found in animal oils. Its empirical formula is $C_{28}H_{43}OH$. **D_3** is produced when *7-dehydrocholesterol* is irradiated. This sterol is found in animal fats, under the skin, etc., and thus D_3 is the form in which vitamin D is found in fish-liver oils and in irradiated milk. Both these varieties of vitamin D have *qualitatively* the same effect in controlling calcium and phosphorus metabolism, and their deficiency will result in rickets. They, however, act differently *quantitatively* in the various species. As an example, D_2 has only a quarter of the efficiency of D_3 upon chickens, but both act equally when tested upon rats.

Vitamin E, which possesses the empirical formula $C_{29}H_{50}O_2$, is an alcohol, *alpha-tocopherol*. It is insoluble in water, but soluble in oils. Absence of this vitamin from the diet of animals causes infertility. In females abortion may occur; in males there is degeneration of the germinal epithelium.

Vitamin K is a fat-soluble substance found in green leaves, especially *alfalfa*, also in pig's-liver fat, and in certain cereals in small quantities. It is essential for maintaining the *prothrombin* content of the blood, and its deficiency gives rise to hæmorrhagic diseases accompanied by reduced coagulability of the blood.

Further information regarding the vitamins will be found summarised in a Table in the *appendix*.

Tissue Oxidation.

In the preceding sections reference has been made to the ultimate disposal of the foodstuffs by stating that they were 'oxidised to CO_2 and H_2O.' This requires some explanation. If some glucose were left exposed to the atmosphere even for days, there would be no evidence that it was becoming oxidised. Yet in the tissues its complete conversion to CO_2 and

H_2O might occur in a few minutes. By some means the oxygen in the tissues has become *activated*. The exact process by which this is conducted, and the factors involved, are still the subject of inquiry, but the following brief summary deals with the more salient points.

A substance may be oxidised, *either* by the addition to it of oxygen, *or* by the withdrawal from it of hydrogen. The addition of oxygen is effected by the presence in all active cells of substances which, in the presence of activating enzymes (*oxidases*), have a great affinity for, and which combine readily with, molecular oxygen. These substances then yield up the oxygen in an *activated* form, and this oxygen can combine with the food products to produce CO_2 and H_2O

An important example of these intermediaries is known as cytochrome. **Cytochrome** is an iron-containing pigment, found in greatest concentration in the tissues which are most active. Chemically it is related to hæmoglobin, and its activity is diminished or abolished by CO and HCN. Schematically its action may be shown as follows:

$$\text{Cytochrome} + O_2\ (+\text{oxidase}) \longrightarrow \text{cytochrome·O}$$
$$\text{Cytochrome·O} + \text{tissue}\ (+\text{oxidase}) \longrightarrow \text{tissue·O} + \text{cytochrome.}$$

For the oxidation of glucose, etc., the presence of **hydrogen acceptors** and an enzyme *dehydrogenase* are necessary. In this case the hydrogen acceptor and the glucose split a water molecule between them. The process may be illustrated in the oxidation of lactic acid to pyruvic acid.

$$\text{Lactic acid} + H_2O\ (+\text{dehydrogenase}) \longrightarrow \text{pyruvic acid} + H_2$$
$$\text{Cytochrome·O} + H_2\ (+\text{oxidase}) \longrightarrow \text{cytochrome} + H_2O$$
$$\text{Cytochrome} + O_2\ (+\text{oxidase}) \longrightarrow \text{cytochrome·O}$$

It will be observed from these examples that the cytochrome is continually changing from the oxidised to the reduced form. By spectroscopic examination these changes have actually been followed in the living cell. In order that oxidation may proceed by the process last outlined, it is necessary, as already stated, that a hydrogen acceptor be present, the cytochrome·O acting in this capacity. **Glutathione** also can act as such, in virtue of the presence in it

of the sulphydryl radical ·SH. Reduced glutathione may be conveniently represented by the letters G·SH. Two molecules, in the presence of water, join together to give the oxidised form G·S—S·G. This can now act as a hydrogen acceptor, becoming once again reduced to two molecules of G·SH.

Animal Heat

A remarkable fact, never yet fully explained, is that the temperature of the human body remains constant within narrow limits. Whether the individual lives in the arctic regions or in the tropics, his temperature is the same. It is evident that the body possesses an astonishingly efficient mechanism for maintaining a steady temperature in spite of variations in the environment. Not all animals are thus provided. A frog in winter has a body temperature almost the same as that of its surroundings; in summer its tissues are warmer, its temperature again depending on the general external temperature. Such an animal is sometimes called cold-blooded, in contradistinction to one which, like man, maintains a steady high temperature. It is better to use the term **poikilothermic** for an animal whose temperature depends on that of its surroundings, animals which have a steady temperature being designated **homoiothermic.** Fishes, amphibians, and reptiles are poikilothermic, birds and mammals are homoiothermic.

The acquisition of a mechanism for maintaining a steady temperature represents a great advance in functional evolution. The activity of poikilothermic animals is largely dependent upon the external temperature (frogs and snakes become torpid in winter and agile in summer). Experiments in the laboratory with skeletal muscle, with cardiac muscle, and with nerves, show that their rate of activity is largely dependent on temperature. Cooling slows physiological processes; rise of temperature up to a certain point accelerates them.

It is known that the rate of all chemical reactions is greatly affected by temperature. Generally speaking, the velocity of any chemical reaction is increased 10 per cent. for each 1° C. rise in temperature. Again,

the viscosity and the surface-tension of all fluids are greatly altered by even a small change in temperature. As physiological processes are largely dependent on chemical changes, and frequently involve the viscosity and the surface-tension of fluids, it will be apparent how a change of body temperature can produce marked differences in the rate of functional activity. It will be further evident why the homoiothermal animal is functionally better equipped.

In mammals we can trace a gradual evolution in the matter of temperature regulation from the lower forms to the higher. The monotremes have a certain power of maintaining a temperature somewhat above that of their surroundings; but this power is by no means perfect. In man alone is the temperature almost constant, the temperature-regulation in monkeys being in turn better than that of the lower mammals—carnivores, rodents, etc. So well is the internal temperature of man regulated that it has been facetiously suggested to use the human body as a thermostat. The temperature level is, however, not absolutely constant. While the mean level is 37·6° C., or 98·4° F., the temperature swings slightly, being half a degree Centigrade lower than this during sleep, and half a degree higher in the afternoon of the waking day.

It is interesting to note that some mammals (homoiothermic) still retain traces of an earlier functional condition as regards temperature regulation. At certain seasons of the year, usually in winter, they lose the power of controlling their temperature, and become for the time being poikilothermic. In this condition, when they are said to **hibernate**, they take the temperature of their surroundings, and are profoundly lethargic, the respirations and rate of the heart-beat being extremely slow, while the reflex and psychic functions of the nervous system are far less active. A similar condition can be produced artificially in any mammal by subjecting it under deep anæsthesia to a low temperature. The shivering reflex being in abeyance, the animal cools down almost as if it were dead. Once the temperature has fallen below a certain point—the ' critical temperature '—the animal, on removal of the anæsthetic, is found to have lost

the power of maintaining a temperature higher than that of its surroundings. If it is warmed above the critical temperature, it immediately begins to shiver and its temperature runs up, but so long as it is kept below the critical temperature it behaves like a hibernating animal.

In a piece of physical apparatus devised to maintain a uniform high temperature (*e.g.*, an incubator), the provision of an automatic 'regulator' ensures that the supply of heat should increase whenever the heat-loss from the apparatus increases, say, owing to fall of the atmospheric temperature. In such a piece of apparatus the conditions are simple, the regulator having merely to vary the supply of heat. In a homoiothermic animal, on the other hand, the mechanism controlled by the 'regulator' is more complicated, and involves means of varying both the *production* and the *loss* of heat.

Regulation of Body Temperature.—The temperature of the body is directly dependent upon the difference between the heat produced *in* the body and the heat lost *from* it. Heat is produced, as has already been seen, by the oxidation of the foodstuffs. This oxidation rises and falls in conformity with the activity of the various organs and tissues. Some glands are always functioning, the muscles are always either contracting or in a condition of 'tone,' therefore heat is *constantly* being produced. Any increased activity will give a greater production of heat. The heat in the body may also be increased by the ingestion of hot foods or drinks.

Heat is *constantly* being lost from the body, (1) by conduction and radiation from the skin, (2) by insensible perspiration, and (3) by the expired air. This air is itself warmed, and it is nearly saturated with water vapour, the vaporisation of which consumes much heat. Heat is occasionally lost from the body by the voiding of urine and fæces.

The balance between heat production and heat loss is controlled by a regulating centre which has not yet been accurately located. It has been suggested that there are *two* centres, one which regulates the balance as above, *thermotaxic*, and the other which controls

heat production, *thermogenic*. If the production of heat should increase above the normal, the cutaneous bloodvessels are dilated, thus allowing more heat to escape from the body owing to a larger volume of the blood approaching more closely to the external atmosphere. If this is not sufficient, then the secretion of sweat is increased, and its latent heat of vaporisation is very effective. Should heat production be less than normal, the cutaneous vessels are constricted, thus conserving the heat. Owing to the restricted circulation in the skin capillaries, the blood becomes venous, thus producing the blueness observed on exposed parts of the body on a very cold day. If, in spite of these precautions, heat is still being lost in excess, then heat *production* is increased. This usually takes the form of **shivering,** which is in reality an increased activity of the muscles, giving rise coincidently to a further output of heat. The *appetite* is also usually stimulated, with the creation of a desire for warm foods, the ingestion of which adds to the heat within the body.

All these methods of control are involuntary. When, however, the balance between heat production and heat loss tends to be greatly upset, voluntary efforts are made to establish equilibrium. Thus heat loss is increased by wearing less clothing, and it is diminished by putting on warmer garments. The protective effect of warm clothing is due chiefly to the layers of air residing in the meshes of the material, which air is a bad conductor of heat. Again, in the tropics, where heat loss tends to be at a minimum, in addition to the wearing of appropriate apparel, efforts are made to reduce the amount of heat production. This is effected by abstaining from work during the hottest hours of the day. Conversely, when the surrounding atmosphere is very cold, in addition to the wearing of heavier clothing, heat production is increased by more muscular activity, such as walking, or ' physical jerks.'

As has been already indicated, a large portion of the body heat is derived from the activity of the muscles. Even when at ' rest ' these tissues are evolving heat, provided their connection with the

central nervous system is intact. During *deep general anæsthesia* this 'tone' in the muscles is almost abolished, and heat production is greatly diminished. Accordingly, during unconsciousness, or when general anæsthetics are being administered, heat loss must be retarded by an increased covering of the body, or by ensuring that it is surrounded by a warmer atmosphere. This is the explanation of the high temperatures obtaining in operating theatres.

CHAPTER XII

THE KIDNEYS AND THE URINE

THE kidney is a compound tubular gland—*i.e.*, its secretory epithelium is arranged in the form of long tubules which in turn are branches of other larger (collecting) tubules. When it is cut open medially it is seen to be formed of two portions—the **cortical** or outer, and the **medullary** or inner. The secretory tubules occur in both portions. In the cortex they are convoluted; in the medulla they lie parallel to each other and form the pyramids of the kidney. Each pyramid has a base abutting against the cortex, and an apex which projects into the upper dilated portion of the ureter, known as the **pelvis of the kidney.**

The **uriniferous tubules** arise in the cortex of the kidney, the point of origin (**capsule** of the tubule) being markedly different in structure from its main length. Throughout the course of the tubule the wall is formed by a basement membrane lined by epithelium, which varies in type in the different parts. The blind end of the tubule is dimpled in like the inverted point of a glove-finger, so as to enclose a tuft or **glomerulus** of convoluted bloodvessels. In addition to the endothelium of the capillaries in the glomerulus, each capillary loop is covered by a layer of the tubular capsule. This capsule consists of a single layer of flattened pavement epithelium, and hence there are only two layers of cells between the blood and the cavity of the renal tract. This peculiar relationship

to the bloodvessels is characteristic of kidney tubules as opposed to those of the sweat glands, and indicates the existence of a very special connexion between the organ and the blood. The combined structure, capsule, and glomerulus is known as a **corpuscle of Malpighi.**

From its point of origin at a glomerulus each tubule, now lined by granular cubical epithelium, pursues a complicated course. After leaving the glomerulus, the tubule, still situated in the cortex, becomes convoluted (**first convoluted tubule**). It then becomes straight, and rapidly narrowing, passes down into one of the pyramids of the medulla as the **descending limb of the looped tubule of Henle,** which is lined by clear flattened epithelium. The tubule might be expected to end here by communicating with one of the large ducts opening at the apex of the pyramid; before reaching the apex, however, it doubles on its course (**loop of Henle**) and passes once more towards the cortex, parallel to its former course (**ascending limb**). The lining is now formed by granular cubical epithelium. Arrived at the cortex, the tubule ap-

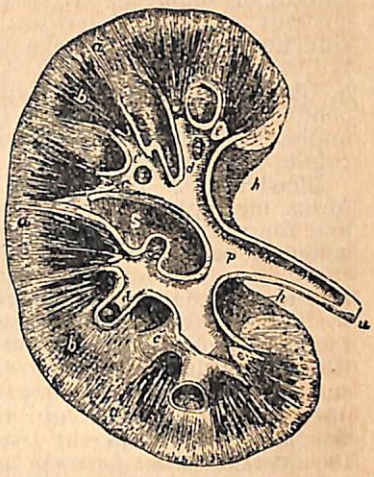


FIG. 30.—PLAN OF A LONGITUDINAL SECTION THROUGH THE PELVIS AND SUBSTANCE OF THE RIGHT KIDNEY.

a, The cortical substance; *b*, *b*, base of pyramids; *c*, *c*, the divisions of the pelvis, named calices, laid open; *c'*, one of them unopened; *d*, summit of the pyramids of papillæ projecting into calices; *e*, *e*, section of the narrow part of two pyramids near the calices; *p*, pelvis or enlarged divisions of the ureter within thed kiney; *u*, the ureter; *s*, the sinus; *h*, the hilum.

proaches close to the glomerulus, from which it took origin, becoming again convoluted (**second convoluted tubule**). Here the lining epithelium is granular cubical, or columnar. Eventually the tubule straightens out again, and narrowing into a small vessel (**junctional tubule**), joins a **collecting tubule,** which unites with others to open at the apex of a pyramid as the **duct of Bellini.** The epithelium in these purely conducting terminal tubules is non-granular in type, and varies in thickness from flattened in the junctional tubule to columnar in the duct of Bellini.

Bloodvessels.—The renal artery, after subdivision, forms incomplete arches lying between the cortex and the medulla in the area known as the **boundary zone** ; the renal vein has a similar distribution. From the convex side of the arterial arches, **interlobular arteries** pass outwards through the cortex, giving off small arterioles (**afferent vessels of the glomeruli**), each of which then divides into a tuft of capillaries (the **glomerulus**), which is received into the inverted end of the capsule of a kidney tubule. The epithelium of the capsule closely invests these capillaries. From the glomerulus an efferent vessel of less diameter than the afferent vessel emerges, and at once breaks up into capillaries, which supply the convoluted tubules of the cortex. The blood from these capillaries is collected by interlobular veins, which join the venous arches in the boundary zone. It is thus seen that in the cortex of the kidney there is a double capillary network (1) in the glomeruli and (2) around the convoluted tubules. The fact that the efferent vessel of the glomerulus, which presumably still contains arterial blood, is smaller than the afferent vessel, indicates that a considerable amount of fluid leaves the bloodvessels and passes into the tubule at the capsule.

The blood to the medulla is now believed to be supplied by the efferent vessels from the glomeruli which are near the medulla. After ramifying in the pyramids, they join again to form venules which enter the venous arches.

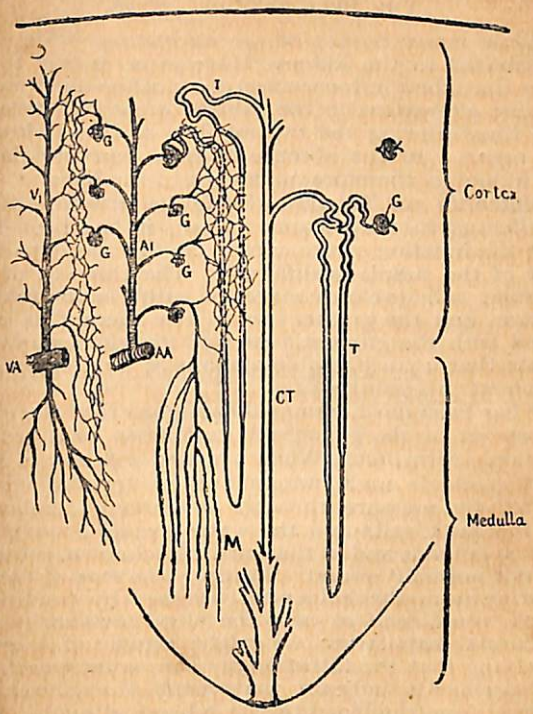


FIG. 31.—DIAGRAM OF THE ARRANGEMENT OF THE BLOODVESSELS AND TUBULES OF THE KIDNEY.

VA, Venous arch; *AA*, arterial arch; V_1, interlobular vein; A_1, interlobular artery giving off afferent vessels to *G*, the glomeruli; *T*, kidney tubule converging on *CT*, one of the main collecting tubules, which opens by a duct of Bellini at the apex of a pyramid; *M*, blood supply to medulla, derived from efferent vessel of glomerulus.

The Secretion of Urine.

While many nerves of the autonomic variety are distributed to the kidney, there is no reason to believe that they influence secretion otherwise than by causing alterations in the calibre of the bloodvessels, and thus altering the rate of flow of blood through the organ. In the absence of true secretory nerves the kidney is therefore analogous to the liver.

Glomeruli and Tubules.—Since the structure of the uriniferous tubule became known, it has been held that the function of the capsule and of the remaining part of the tubule is different. The thinness of the capsular wall, its close connection with a large capillary surface, and the greater size of the afferent as compared with the efferent vessel of the glomerulus, indicate that a considerable amount of fluid enters the tubule at this point.

It has been most commonly assumed that the urine passes out of the glomerular capillaries by a process of simple filtration. When a mixed solution of proteins (colloid) and inorganic salts (crystalloid) is filtered by pressure through an animal membrane, the inorganic salts and the water exude, leaving the protein behind; and in the urine, as is known, proteins are not normally found. Further, the rate of escape of urine from the kidney is increased by conditions which would tend to raise the blood-pressure in the glomerular capillaries; we might explain this result by saying that the filtration pressure is increased.

Experiments indicate that many substances are secreted from the blood by the cubical cells which line the lumen of the tubule. Thus, in birds, when the ureters are ligatured, urates are found lying in the convoluted tubule, not in the capsule. Also if acid fuchsin is injected into the blood, the convoluted tubules are found red, the capsule colourless. Acid fuchsin is decolorised by alkali, remaining red only in the presence of acid. The experiment indicates that the convoluted tubules secrete acid constituents.

Theories regarding Secretion.—Many different views have been advanced as to the exact manner in which

urine is formed in the kidney, and the main theories are probably best studied chronologically.

In the middle of the seventeenth century **Malpighi** noted the presence of ' corpuscles ' in the kidney, and he regarded them as secretory glands in which the urine was elaborated from the blood. No one offered an alternative explanation until 1842, when **Bowman** came forward with his theory. He considered that the glomeruli served as filters which allowed water to pass into and along the tubules, where it dissolved the urinary constituents that had been actively secreted in a more or less solid form by the tubule cells. This hypothesis had hardly been assimilated before **Ludwig** came forward with an alternative view in 1844. He held that the glomerulus acted in a purely passive manner to filter off water containing all the plasma constituents except the proteins. This fluid then passed along the tubules, where passive absorption occurred until it had the constitution of urine. In 1874 **Heidenhain** put forward a modification of Bowman's theory whereby he suggested that the whole process in the kidney was an active rather than a passive one, and that water with a low salt content was secreted by the glomerulus and passed on to dissolve a solid secretion of the remaining urinary constituents in the tubules. Little advance was made on these views until 1917, when **Cushny** came forward with his theory. Cushny divided the constituents of the urine into two groups, (*a*) threshold, and (*b*) non-threshold.

Threshold substances are those which are passed out into the urine only when they rise above a definite level in the blood. Cushny held that these substances are reabsorbed from the fluid passing through the tubules until their amounts in the blood rise to their respective threshold values. Examples are potassium, sodium chloride, glucose and amino-acids. All these substances are useful in the body metabolism.

Non-threshold substances are those which are waste products or are useless for metabolic purposes and which are passed out no matter how low their amount in the blood. Such substances are not re-

absorbed at all in the tubules, and they include urea, creatinine, and sulphates. In support of this theory is the fact that microdissection has shown that in the frog's kidney the urine in the glomerulus contains constituents (*e.g.*, sugar, etc.) which are not present in the bladder urine, and which must therefore be absorbed in the tubules.

In 1925 **Starling and Verney** modified Cushny's theory with the suggestion that, whilst reabsorption of threshold substances occurred in certain parts of the tubules, *secretion* of some other of the constituents took place elsewhere in the tubules. At the present time the evidence is not considered sufficient by which to arrive at a definite conclusion as to the function of the tubules.

The different theories are summarised below:

Name.	*Function suggested for—*	
	(*a*) *Glomerulus.*	(*b*) *Tubule.*
Bowman (1842).	Water filtration.	Active secretion of the urinary constituents in solid form.
Ludwig (1844).	Passive filtration of water and all plasma constituents except the proteins.	Passive absorption.
Heidenhain (1874).	Active secretion of water with low salt content.	Solid secretion of urinary constituents.
Cushny (1917).	Passive filtration of water and all plasma constituents except the proteins.	Active reabsorption of threshold substances.
Starling and Verney (1925).	As Cushny.	Double function—one part being absorptive and the other part secretory.

Micturition.—The secretion of urine, like that of the bile, is continuous. The fluid is carried along the ureters by peristaltic contractions of their walls, escaping into the urinary bladder by drops. Both

ureters and bladder contain a muscular coat of plain muscle tissue. At the cervix of the bladder a number of fibres running in a circular direction function as an internal sphincter. These muscles are supplied by nerves arising from two sources: (*a*) sympathetic, coming from the first two lumbar segments of the spinal cord, and causing, on stimulation, contraction of the internal sphincter and also closure of the ureteric openings; (*b*) parasympathetic, coming from the second and third sacral segments. On stimulation of these latter fibres the general muscle of the bladder wall (detrusor) contracts, the internal sphincter relaxes, and the bladder is emptied. It is believed that the afferent fibres from the bladder accompany both these sets of fibres to the lumbar and sacral segments of the cord. It has been shown that the muscular wall of the bladder maintains a certain tone, so that there is a constant pressure maintained in the bladder, whether it is well filled or almost empty. This pressure is approximately equivalent to 15 cm. of water. When the bladder begins to become really full, the pressure gradually rises, and when it reaches 18 cm. of water afferent impulses pass to the spinal centre and up to the cerebral cortex, and one feels the desire to micturate. From there messages are sent down the cord to stimulate the parasympathetic nerves, with effects as above. When the *bladder* is irritable—as, for example, in infections of the urinary tract—the afferent impulses are initiated at a much lower pressure. This explains the frequency of micturition that occurs in such cases. The irritability of the *centre* may be increased by emotional conditions, thus giving rise to the desire to micturate, even when the bladder contains little or no urine. By voluntary effort the process of micturition can be delayed for a time. This is accomplished by the contraction of an external sphincter, composed of striated muscle situated just outside the bladder and controlled by the cerebral cortex. It is also possible to accelerate the outflow of urine. This is effected by simultaneous contraction of the diaphragm and abdominal muscles. Occasionally, and especially after con-

siderable distension, the plain muscle of the bladder does not keep pace with the outflow of the fluid, the desire to micturate then ceases, to return after a minute or so, when the bladder has, as it were, taken up the slack.

It will be seen therefore that micturition is fundamentally a spinal reflex, regulated by the cerebrum. The spinal centre is situated in the 2nd and 3rd sacral segments. When this is destroyed by accident or by disease, the urine dribbles out continuously from the urethra, the periodic action of the bladder being abolished. Any lesion of the spinal cord above this level does not interfere with periodic micturition, but abolishes the voluntary control of the bladder, and also one can no longer appreciate when it is necessary to micturate.

The Urine.

Urine is a clear yellowish fluid, having an aromatic odour, acid reaction, and a specific gravity of 1·015 to 1·025 at 15° C. If the specific gravity is taken at any other temperature, the reading should be corrected by adding or subtracting 0·001 for each degree above or below 15° C. respectively.

The acidity, due to the presence of acid sodium phosphate (NaH_2PO_4), varies during the day. After a meal the urine may react alkaline. The secretion of hydrochloric acid into the stomach tends to render the blood more alkaline, with the result that less organic acid and more disodium—*i.e.*, alkaline phosphate (Na_2HPO_4)—appears in the urine. When a considerable quantity of disodium as well as of acid phosphate is present, the urine may act upon blue as well as on red litmus—**amphoteric reaction.** The acidity of the urine can be estimated approximately by titrating with a decinormal solution of caustic soda, using phenolphthalein as an indicator. When kept for a day or two, urine acquires an alkaline reaction from ammoniacal fermentation, owing to infection with the *Micrococcus ureæ*, which breaks down the urea into ammonium carbonate. If the bladder becomes infected with the *Micrococcus ureæ*,

owing, for example, to the passage of a non-sterile instrument, ammoniacal fermentation may occur in the viscus, the excreted urine then reeking of ammonia.

The amount of urine daily excreted by the adult varies between 1,200 and 1,800 c.c., the average being about 1,500 c.c. The quantity, however, is greatly influenced by a number of conditions, such as the amount of the fluid intake. On a warm summer day, when perspiration is active, only small quantities of highly concentrated urine may be voided.

COMPOSITION.—The urine contains many inorganic salts and various organic substances, all of which are crystalloid. Though colloidal substances are largely present in the blood, no measurable amount of colloid appears in the urine unless the kidney is diseased.

The chief inorganic salt is sodium chloride, about 12 to 16 grammes being excreted per diem. It is derived directly from the salt taken with the food, its chief function in the blood and in the tissues being to maintain proper conditions of osmotic pressure. If sodium chloride is withheld from the food its excretion in the urine almost stops, the available supply being retained in the blood and tissues. If large amounts of sodium chloride are given, thirst is produced, more fluid is drunk, and the salt with large amounts of water is thrown out by the kidney. Phosphates and sulphates are also present in the urine. These do not necessarily enter the body in this form. For one thing, the inorganic sulphates are acrid, bitter substances which, even in small quantity, would make the food unpleasant. Phosphates again are quite palatable, but not very abundant in food. Phosphorus and sulphur, however, form important constituents of many proteins; therefore, it is easy to understand that some of the phosphate in the urine and practically all the sulphate result from oxidation within the body. The phosphates are combined either with univalent sodium or potassium, or with divalent calcium or magnesium, the latter compounds being known as earthy phosphates. All phosphates are soluble in acid solution, and in normal fresh urine the phosphates are dissolved. In alkaline

solution the earthy phosphates are precipitated, and when urine has stood for a time, they fall out. The same result occurs when the bladder is accidentally infected with the *Micrococcus ureæ*, the voided urine being turbid and phosphatic calculi being apt to form in the bladder.

Sulphur is excreted mainly in two forms: (1) completely oxidised as sulphate, which is either inorganic or ethereal; (2) in organic combination as so-called 'neutral' sulphur. All the sulphur enters the body in organic combination with the protein food. The inorganic sulphates are combined with inorganic bases, the bulk of the sulphate occurring in this form.

The substances phenol, indole, and skatole are produced by putrefaction in the large intestine, and if the last two are absorbed into the blood they are oxidised into indoxyl and skatoxyl respectively. The phenol, indoxyl, and skatoxyl, combining with sulphuric acid, form the ethereal sulphates. These are normally present in the urine only in small amounts, but are largely increased in chronic constipation. 'Neutral sulphur,' which is not oxidised, occurs very rarely, as in cystine.

The chief nitrogen-containing substances in the urine are urea, ammonia, uric acid, and creatinine; the bulk of these are protein derivatives, the uric acid, however, being obtained chiefly from nucleoproteins (see p. 137).

The most important nitrogenous constituent is urea or carbamide—$CO(NH_2)_2$—its nitrogen forming on an average 80 to 85 per cent. of the total nitrogen in the urine. It is formed chiefly in the liver from the metabolism of proteins, and increases in amount with increasing intake of protein food. Urea forms approximately 2 per cent. of the urine, and hence about 30 grammes are excreted per day.

While the ammonia formed from the deamination of amino acids in the liver is chiefly converted into urea, a certain amount combines directly with acids and is excreted in the urine as ammonium compounds, 0·6 to 1 gramme being the average daily amount thus thrown out. There is an increase in the am-

monium compounds, with a corresponding decrease in the urea (*a*) if mineral acids are given with the food, or (*b*) if there is an increased production of acid in the body as a result of disordered metabolism, such as in diabetes.

Uric acid, which is an end product of purine metabolism, is derived partly from an exogenous, partly from an endogenous, source, and is present to the extent of 0·3 to 1·6 grammes. It forms salts known as urates, of which there are three forms, the commonest being quadriurates.

Creatinine is entirely of endogenous origin. The amount excreted per day (about 0·9 gramme) is a measure of tissue metabolism. The reducing action of concentrated urine on Fehling's solution is partly due to creatinine (also to uric acid). The allied substance, creatine, is found only exceptionally—*e.g.*, in the urine of children and of pregnant women.

Besides these, other nitrogenous substances—*e.g.*, hippuric acid, amino acids, and indican—occur in traces.

The urine contains a number of pigments, its yellow colour being due to urochrome, which, like urobilin, is probably derived from bile pigments. Urobilin is increased in amount in certain liver diseases—*e.g.*, cirrhosis. Other pigments, uroerythrin and hæmatoporphyrin, also occur, the latter in large amounts in cases of sulphonal poisoning.

Abnormal Constituents of the Urine.—In pathological conditions abnormal substances appear in the urine. These may include materials such as protein, bile, sugar, which under ordinary conditions do not pass the kidney epithelium. Formed elements such as blood corpuscles and kidney epithelium may also appear in abnormal conditions. Products of the intermediary metabolism of the foodstuffs —*e.g.*, amino acids, oxy-fatty acids, cystine, homogentisic acid, creatine, may sometimes be found. The proteins usually found are serum albumin and serum globulin; their presence (**albuminuria**) indicates kidney disease, in which the tubules are unable to hold back the colloids of the blood. In one peculiar

condition a hetero-proteose, known as Bence-Jones protein, is excreted. Small quantities of blood in the urine darken its colour and render it 'smoky'; in larger amount blood may tinge the urine red. The presence of blood is known as **hæmaturia,** and is due to bleeding from any part of the urinary tract. More rarely the same kind of appearance may be produced by hæmoglobin in solution with no red blood corpuscles. This condition, known as **hæmoglobinuria,** is associated especially with hæmolysis. Methæmoglobin may also appear in the urine, as in blackwater fever.

The chief sugar excreted in pathological conditions is glucose. **Glycosuria,** associated with hyperglycæmia, is characteristic of the disease diabetes mellitus, in which other substances, aceto-acetic acid (ketonuria), oxybutyric acid, and acetone (acetonuria), may also be excreted. Besides glucose, other sugars may occur, only more rarely; thus, lactose (lactosuria) may appear in the urine of women at a late stage of pregnancy. Lævulose and pentose have also been described in the urine.

Alkaptonuria is a condition in which homogentisic acid, an aromatic acid, appears in the urine, and is due to an inborn error of metabolism affecting the breaking down and the ultimate disposal of the tyrosine constituent of the proteins.

URINARY DEPOSITS.—The commonest deposit is mucus, which may occur in acid as well as in alkaline urine. Most deposits, however, are influenced by the reaction of the fluid. (1) *In acid urine,* uric acid, urates, calcium oxalate, and cystine are not infrequent deposits. The uric acid crystals are pigmented and give an appearance as if cayenne pepper had been sprinkled on the sides of the containing vessel. Urates are thrown down as a rule as a brick-red amorphous deposit, which dissolves on warming the urine. It is to be noted that the colour of the uratic deposit is due to its affinity for the urinary pigments, and if these latter are scanty or lacking, the deposit is pale yellow or even colourless, and therefore may be superficially mistaken for phosphates. Calcium

oxalate is white, the crystals appearing under the microscope as 'envelopes.' (2) *In alkaline urine*, triple or ammonio-magnesium phosphate; stellar or calcium-hydrogen phosphate ($CaHPO_4$); and ammonium urate may be found. Triple phosphate, the crystals of which have frequently a coffin-lid shape, may also occur in slightly acid urine. All crystals of phosphate are dissolved on the addition of acid in any quantity.

The above deposits are all unorganised. Organised deposits, such as blood corpuscles, pus cells, bacteria, and casts of the kidney tubules may result from certain pathological lesions.

Urinary calculi may consist of uric acid, of calcium oxalate, or of earthy phosphate, with which in each case may be mingled organic substances such as cystine or cholesterol. Uric acid and calcium oxalate calculi can be deposited only in acid urine; the medical treatment of these consists in attempting to reduce the acidity of the urine. Phosphatic calculi can form only in alkaline urine, and are specially prone to occur in the bladder infected by the *Micrococcus ureæ*.

CHAPTER XIII

THE SKIN AND ITS FUNCTIONS

The Skin and its Appendages.

The skin consists of a superficial epithelial layer—the **epidermis**; and of a tough fibrous tissue—the **dermis**; this passes by insensible degrees into ordinary areolar and adipose tissue—**subcutaneous tissue.**

The epidermis consists of stratified squamous epithelium: the cells of the outer layers are mostly dead, flattened, and horny—the **stratum corneum**; this is thickest where the surface of the body is subject to intermittent pressure, as on the soles of the feet and on the palms. The superficial layers of

the stratum corneum are constantly being worn away and shed, and are renewed from the deeper portion of the epidermis, the **rete mucosum (Malpighian layer).** The rete mucosum consists of a layer of columnar cells next the dermis and a superficial granular layer—the **stratum granulosum.** Between the latter and the stratum corneum is a thin layer which appears transparent in section—the **stratum lucidum.** These layers are merely transitional conditions of the cells between the Malpighian layer and the stratum corneum.

THE DERMIS (**cutis vera**) consists of fibrous connective tissue, passing by insensible degrees into the subcutaneous areolar and adipose tissue. Its surface is covered with microscopic **papillæ,** which project upwards into the epidermis. The dermis is richly supplied with bloodvessels and nerves, exhibits tubular depressions in which the roots of the **hairs** are lodged, and has a vast number of glands which open upon the external surface—**sweat glands**—or into hair follicles —**sebaceous glands.**

The papillæ attain their maximum development on the lips and those parts which have the greatest tactile sensibility. Each papilla contains either a capillary plexus or a special sensory nerve termination.

The most important of these terminations are the **tactile corpuscles, end bulbs, Pacinian corpuscles,** and **organs of Ruffini.** They all consist of a connective tissue capsule (an expansion of the perineurium) enclosing a soft protoplasmic core (corresponding to endoneurium). Within the core the *axis-cylinder* terminates either simply or by an arborescence.

TACTILE CORPUSCLES are found chiefly in the papillæ of the fingers and toes, where tactile discrimination is highly developed.

END BULBS occur in the conjunctiva of the eye, the papillæ of the tongue and in serous membranes. In a modified form they are found in the mucous membranes of the external genitals.

PACINIAN CORPUSCLES are very large and have a special formation. The connective tissue capsule is disposed in concentric laminæ. The axis-cylinder,

enclosed in a cylindrical core of endoneurium, passes through the length of the capsule to end in aborisations. Pacinian corpuscles occur abundantly in the deep layers of the dermis of the hands and of the feet, on the nerves of the periosteum and of the joints.

ORGANS OF RUFFINI exhibit a long cylindrical

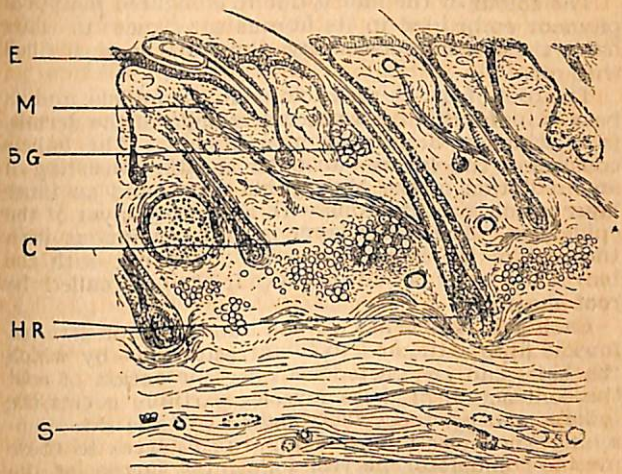


FIG. 32.—SECTION OF SKIN.

E, Epidermis; M, arrector muscle of hair; SG, sebaceous gland; C, cutis vera; HR, hair root; S, subcutaneous tissue, with bloodvessels, nerves, etc. (Walsh, 'Diseases of the Hair.')

capsule, and occur in the subcutaneous tissue of the human finger.

The above are receptors of the sensations of touch, pain, heat and cold, but the particular function of each type has not yet been fully defined.

The appendages of the skin are the **hair, nails, sweat glands,** and **sebaceous glands.** They are all modifications of the epidermis.

HAIR.—A hair consists of a bulbous **root** embedded in a follicle of the dermis, and of a **shaft** which ter-

minates in a fine point. The shaft consists of fine **fibres,** arranged in the direction of the axis of the hair; these are formed of elongated cells cemented together. It is covered with minute **imbricated scales,** which overlap like tiles. Some of the larger hairs have a central cavity filled with spheroidal cells.

The **colour** of the hair is due to elongated masses of pigment embedded in its fibrous substance; in white hairs these are replaced by numerous lacunæ filled with air.

The root of the hair is enclosed in the **follicle,** and its base is perforated by a **vascular papilla** of the **dermis,** from which it derives its nourishment. The follicle consists of **two layers**—an **outer sheath,** consisting of an involution of the Malpighian layer, and an **inner layer** which is continuous with the horny layer of the epidermis. The inner layer is also continuous with the root of the hair—it usually comes out with the hair if the latter is pulled; hence it has been called the **root sheath.**

Each hair follicle has a small bundle of non-striated muscle fibres attached to it—**arrector pili**—by which the hairs can be erected. Under the action of cold the contraction of these muscles partially everts the follicle, and produces the roughness of the skin commonly known as '**goose skin.**' The nerves to these muscles, **pilomotor nerves,** follow the course of the vaso-constrictor nerves.

NAILS.—The nail is composed of keratinised cells derived from the stratum corneum. It rests on a furrowed bed formed by the dermis, and its posterior portion, the root of the nail, is lodged in a fold in the epidermis. This fold overlaps the root of the nail to form the cuticle. Growth is effected by the addition of cells to the under surface and to the root of the nail. The nail bed is very vascular and well supplied with nerves. The **lunula,** a small white crescent at the root of the nail, is due to the dermis being less vascular at this spot than under the rest of the nail.

SWEAT GLANDS.—Each gland consists of a simple tube, divided into a **glandular part,** which is coiled upon itself and lies in the subcutaneous tissue, and

into an **efferent duct,** which pierces the dermis and makes its way in corkscrew fashion through the epidermis. The convoluted glandular part consists of a basement membrane lined by a single layer of cubical glandular epithelium. The efferent duct, much thinner, is lined by two or three layers of cells.

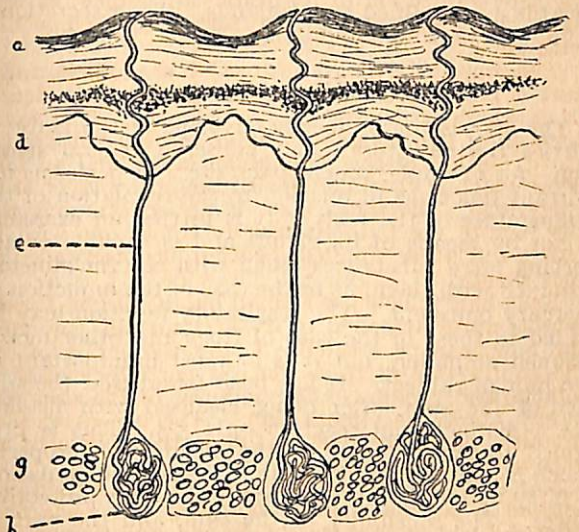


FIG. 33.—DIAGRAMMATIC SECTION THROUGH THE SKIN, SHOWING THE SWEAT GLANDS AND THEIR DUCTS.

a to *d*, Epidermis; *d*, papillæ; *e*, sweat ducts; *d* to *g*, dermis; *g*, subcutaneous fat; *h*, sweat glands.

Sweat glands occur all over the skin, being especially numerous on the palm of the hand and on the sole of the foot. Very large sweat glands occur in the axilla.

SEBACEOUS GLANDS are composed of simple pouches, opening by ducts into the hair follicles. They are lined throughout with spheroidal cells. The sebaceous secretion, consisting of fatty matter and

cholesterol, is formed by disintegration of the epithelial cells in the gland. It serves to lubricate the hairs, and to form a thin protective covering on the skin which tends to prevent undue evaporation of water.

THE MEIBOMIAN GLANDS in the eyelids are a modified form of sebaceous glands.

THE CERUMINOUS GLANDS of the external auditory meatus are modified sweat glands. Their secretion is a mixture of sebum and sweat.

FUNCTIONS OF THE SKIN.

The skin is the **protective** envelope of the body; it carries the receptors which subserve general **sensation**—for example, touch, pain, etc. It performs important functions in relation to the regulation of the **temperature** of the body. It is further an **excretory** organ by means of its glands and is capable of **absorbing** fatty substances along with certain minerals admixed with them, as in the case of the inunction of mercury ointment. The **respiratory** function may be added to these in the case of **frogs** and other moist-skinned amphibia, but it is at most unimportant in the human subject. It has been found that the surface of the skin, after being cleansed with alcohol, has a distinct acid reaction—pH 5·5. This is presumed to be the cause of the disinfecting property which is exhibited by the skin. Dirt or accumulation of fatty material on the surface lessens this protective power. The sensibility of the skin, and the part it plays in the regulation of temperature, are considered in other sections of this book.

THE SWEAT consists chiefly of **water** with the **salts** of the blood in solution (less than 2 per cent. of solids). It has a faintly acid reaction and a low specific gravity. The chief constituent is NaCl, which is present in a concentration of from 0·06 to 0·5 per cent. An undue amount of NaCl may be lost when there is excessive and prolonged sweating. This loss is said to be the cause of the so-called **water poisoning** occurring in workers in deep mines, steel works, etc. This condition exhibits violent muscular cramps and

an intense thirst. Urea is also present in quite perceptible amount. When the function of the kidneys is interfered with, as in Bright's disease, the sweat glands may eliminate large amounts of urea.

The **quantity** of the secretion formed is subject to very great variations and depends much upon the surrounding conditions. It may vary from 0·5 to 1·0 litre per day in an adult at rest, to as much as 2·5 litres in *one hour* during strenuous muscular activity. When the air is warm and dry, the sweat evaporates from the skin as fast as it is formed, and is spoken of as **insensible perspiration**; in a moist atmosphere, and when the secretion is very copious, it collects upon the skin, or runs down in drops; it is then spoken of as **sensible perspiration.**

THE NERVOUS MECHANISM OF PERSPIRATION.—The relation of the secretion of perspiration to the temperature of the body, and the amount formed, is under the control of the central nervous system. The centre has not been definitely located. An increased supply of blood to the skin, the result of **vasomotor inhibition,** acts only indirectly in increasing the secretion, which is under the direct control of special **secretory nerves.**

In the cat and dog sweat glands are present chiefly in the pads of the feet. If the sciatic nerve of one of these animals is cut and its peripheral end stimulated, beads of perspiration begin to appear on the pads of the foot, especially if the foot is kept moderately warm. From this we conclude that the secretory nerves run in the sciatic. Mere exposure of the foot of an intact animal to a high temperature causes perspiration; in this case the secretion is stimulated reflexly through the central nervous system. Secretory fibres belonging to the sympathetic system leave the spinal cord in the thoracico-abdominal region as pre-ganglionic nerves, which synapse in co-lateral sympathetic ganglia, from which post-ganglionic fibres proceed by way of the mixed nerves to the glands.

The sweat glands are peculiar in that although they are supplied by sympathetic nerves, the injection of adrenaline does not stimulate the glands. This is

because the post-ganglionic fibres supplying the glands are *cholinergic* (p. 216). The injection of pilocarpine, which is a *parasympathetic* stimulant, produces a copious secretion of sweat. Neither this secretion nor that following stimulation of the sympathetic nerves will occur if atropine has been previously injected.

CHAPTER XIV

THE NERVOUS SYSTEM

I. The Spinal Cord.

The spinal cord consists of **white matter,** superficially situated, and of **grey matter,** which lies more deeply.

The grey substance is seen in transverse sections in the form of two crescents placed back to back, and united by a **commissure,** so that it somewhat resembles the form of the letter **H**. In the centre of this commissure is a minute canal lined with ciliated columnar epithelium, the **central canal of the cord.** The grey substance is entirely surrounded by the white substance.

The whole cord is divided into two lateral halves by the **ventral** (anterior) and **dorsal** (posterior) **median fissures ;** each half is further marked by two grooves each in a line with the ventral and dorsal nerve roots respectively. Thus the lateral halves of the cord are divided into three parts, a **lateral column** situated between the nerve roots, a **ventral column** in front of the ventral nerve roots, and a **dorsal column** behind the dorsal nerves.

The cord lies in the spinal canal of the vertebral column, and is enveloped in three membranes—dura mater, arachnoid, and pia mater, from without inwards.

The **white substance** of the spinal cord consists of **medullated nerve fibres** devoid of primitive sheaths, the greater number of which run longitudinally, together with ordinary connective tissue, neuroglia, and blood-vessels. In transverse stained sections, the fibres

appear as clear rings with a central stained dot—the transverse section of the axis cylinder. The **grey substance** consists of (1) an abundant neuroglia, permeated by a fine capillary network, in which (2) a great number of **nerve cells** and their dendrons are embedded, and (3) a fine reticulum of delicate axis cylinders and their collaterals. The nerve cells are arranged in distinct columns—vesicular columns—which appear as groups of cells in transverse sections.

THE REGIONS OF THE SPINAL CORD.—Every portion of the cord is connected to the brain by nerve fibres

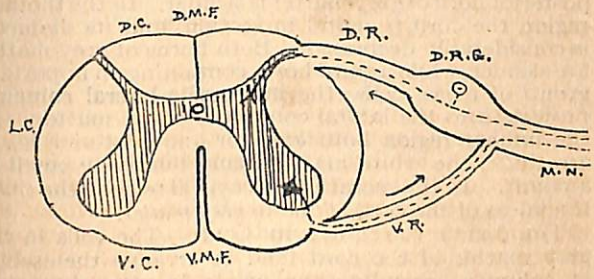


FIG. 34.—SECTION OF CORD, SHOWING PARTITION INTO COLUMNS, AND ORIGIN OF SPINAL NERVE-ROOTS.

D.M.F., dorsal median fissure; *V.M.F.*, ventral median fissure; *D.C.*, *L.C.*, *V.C.*, dorsal, lateral and ventral columns, respectively; *D.R.*, *V.R.*, dorsal and ventral nerve-roots; *M.N.*, mixed nerve; *D.R.G.*, dorsal root ganglion.

(white matter). These fibres run in the cord, and therefore they are present in greatest amount the nearer the cord approaches to the brain. By this difference in the amount of white matter alone we can distinguish a section, say, of the cervical region from one of the lumbar region. Apart from the characteristics conferred by the relative amount of white matter, there are two marked enlargements of the cord, one in the cervical, the other in the lumbar region. These correspond with the outflow of nerves to the upper and lower limbs respectively. In each of the enlargements the amount of grey substance is

much increased, owing to the presence of a greater number of nerve cells.

Sections through the different regions may be distinguished as follows: In the upper **cervical regions** the white matter is abundant, and the lateral column of white matter is invaded by a network of a grey substance (**formatio reticularis**). In the cervical enlargement the anterior horn of grey matter is especially thick. Throughout the cervical region the posterior columns of white matter are each subdivided by a septum into a median and lateral portion, and the posterior horn of grey matter is slender. In the **thoracic region** the cord is round in section, and its diameter is considerably decreased. Both horns of grey matter are slender, while a third horn, containing an important group of nerve cells (the **intermedio-lateral column**), projects into the lateral column of white matter. In the **lumbar region** both anterior and posterior horns are thick, the white matter being relatively small in amount. In the **sacral** and coccygeal regions the main thickness of the cord is due to *grey matter*.

THE NERVE CELLS OF THE CORD.—The cells in the grey matter of the cord tend to arrange themselves in columns extending the whole length. In cross-section these columns appear as *groups*, and they are sometimes referred to as such. Four main groups have been demonstrated, two concerned with efferent, two with afferent, impulses.

The **ventral horn cells,** which are stellate in shape, are found, as their name indicates, in the anterior horn. Their axons, which form the motor fibres found in the ventral nerve roots, pass direct to the skeletal muscles. In the cervical and in the lumbar enlargements these motor cells occur in clusters corresponding to movements of the limb-segments; thus there are flexor and extensor groups respectively. The cells that innervate the shoulder and hip respectively lie at a higher level than those connected with the muscles of the hand and of the foot. The **intermedio-lateral column** of cells is found in the lateral horn of grey matter in the dorsal region. These cells are round in shape, and their axons form the medullated

pre-ganglionic fibres of the *sympathetic* nerves (*q.v.*). They pass out of the cord in the ventral nerve root to reach their respective ganglia, whence messages are conveyed to the plain muscle of the viscera and the bloodvessels.

Another well-marked group of nerve cells (**Clarke's column**) is found chiefly in the thoracic region, where it lies at the base of the posterior horn. The axon processes of these cells run upwards in the lateral region of the cord to end in the cerebellum. They carry 'unconscious' sensations from joints, tendons and muscles, and are concerned with the maintenance

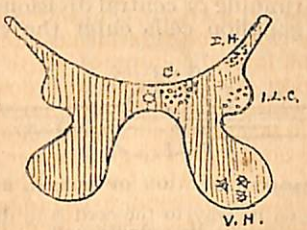


FIG. 35.—DIAGRAMMATIC SECTION OF GREY MATTER IN DORSAL REGION OF CORD TO SHOW POSITION OF CELL GROUPS.

C., Clarke's column; *D.H.*, dorsal horn cells; *I.L.C.*, intermediolateral column; *V.H.*, ventral horn cells; *C.* and *D.H.* give rise to afferent fibres, the others to efferent fibres.

of equilibrium. A less well-defined cluster of cells is found near the extremity of the dorsal horn, and is known as **dorsal horn cells.** The axon processes of these cross in the ventral commissure, and convey impulses of pain, heat and cold to the optic thalamus (Fig. 35).

THE SPINAL NERVE-ROOTS.—Each spinal nerve arises by the union of two roots, a ventral and a dorsal. The **ventral nerve-root** contains only efferent fibres, which come from the motor nerve-cells in the anterior horn (supplying skeletal muscles) and from cells of the lateral horn (supplying plain muscle). The **dorsal root,** the fibres of which are mainly afferent, is dis-

tinguished by the possession of a ganglion. This ganglion or swelling is occasioned by the fact that at this spot there are collected together the cells which give rise to the fibres of the dorsal root. These cells are unipolar, and the single axon process of each cell divides in a T-shaped manner (see Fig. 6, p. 25, and Fig. 36) into two fibres, one of which runs into the cord, the other being continued peripherally along the mixed nerves to a sensory nerve organ. All nerves of common sensation, whether they enter the spinal cord or the brain, are similarly derived from round unipolar nerve-cells, situated in a ganglion close to the point of entry of the corresponding nerve-root.

The inward-running or central divisions of the axons of the spinal ganglion cells enter the cord near the

FIG. 36.—DIAGRAMMATIC SECTION OF DORSAL ROOT GANGLION. Each nerve fibre on its way to the cord is in direct continuity with its unipolar cell.

dorsal horn of grey matter, where each divides into a short descending and a longer ascending branch. Some of these ascending branches end by synapsing round cells of the cord at a higher level; others, however, travel upwards as far as the medulla oblongata. The descending branches all synapse around nerve-cells of the cord. Throughout their upward or downward course these fibres give off smaller branches or **collaterals,** which also connect with nerve-cells (Fig. 37).

Section of the ventral roots gives rise to paralysis of the muscles, section of the dorsal roots to a loss of sensation.

CONDUCTION IN THE SPINAL CORD.

Any single segment of the cord is connected with external sense-organs by means of fibres entering by the dorsal nerve-roots, and with skeletal muscle, plain

muscle and glands, by means of efferent fibres *via* the ventral nerve-roots. It is also connected with other segments of the cord and with the brain by fibres which arise in the cord itself, called **proprio-spinal fibres.** The proprio-spinal fibres which connect neighbouring

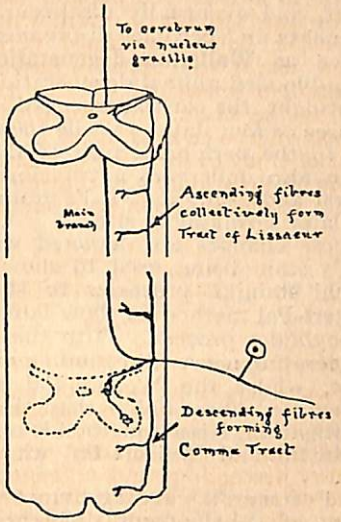


FIG. 37.—DIAGRAM TO SHOW THE MODE OF ENDING OF A SENSORY NERVE FIBRE IN THE SPINAL CORD.

On entering the cord the fibre divides into two divisions, ascending and descending. The descending division is *short*; the ascending is *long* and may continue as far as the brain (medulla oblongata). Each division gives off collaterals which synapse with cells in the cord.

segments of the cord are deeply placed in the white matter, those which connect distant segments being more superficial.

The Course of these nerve-tracts and their origin from particular nerve-cells has been determined by one or other of the following methods:

1. Degeneration of Nerve and Chromatolysis.—When the axon process of a nerve-cell is cut across, the peripheral part of the nerve fibre undergoes degeneration throughout its whole length (see p. 27). The myelin sheath of each internode, losing its continuity, is first transformed into spherical or ellipsoidal droplets of fat, and eventually disappears; the axis cylinder fragments and becomes disorganised. This process is known as **Wallerian degeneration** of nerve. In a warm-blooded animal degeneration is far advanced in a fortnight, the earliest traces of it being quite visible in three or four days. While these changes are occurring in the peripheral part of the nerve, the cell of origin also undergoes a transformation, swelling up at first and losing its Nissl's granules (**chromatolysis**), and later shrinking in size.

These changes are detected with the microscope, **Nissl's** stain being used to show chromatolysis, the **Marchi** staining processes to show early, and the **Weigert-Pal** method to show late degeneration of the axis-cylinder process. With the Marchi method the degenerating nerve fibres stain *darker* than the normal nerve, whilst the Weigert-Pal method shows the degenerated fibres *lighter* than the rest. For routine investigation, Nissl's method is not practicable, those of Marchi and Weigert-Pal are employed successfully.

2. Flechsig's Myelination Method.—In the course of development different conducting tracts acquire their myelin sheaths at different periods. Generally speaking, sensory tracts become myelinated at an earlier stage than efferent or motor tracts. By cutting sections of the cord at different stages of embryonic and post-embryonic development, and staining them by the Weigert-Pal method, we can pick out each new tract as it appears in successive order.

Spinal Pathways.

Investigation has shown that the white matter of the cord can be divided into two main divisions, the **ascending tracts,** conveying impulses upwards to higher

regions in the cord or to the brain; and **descending tracts,** which convey messages in the reverse direction.

THE ASCENDING TRACTS.—These are known as exogenous or endogenous, according to whether they arise from cells of the spinal ganglion or from cells of the cord. The chief **exogenous** tracts are the **tract of Goll** (*fasciculus gracilis*) which goes to the nucleus gracilis of the medulla oblongata, the **tract of Burdach**

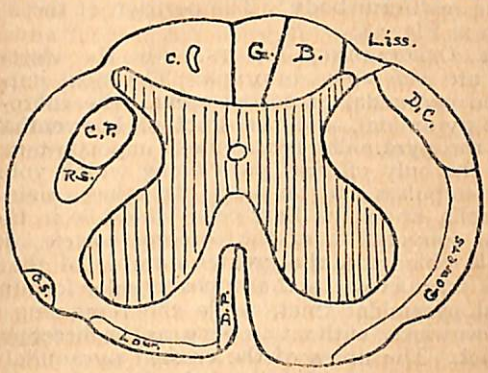


FIG. 38.—SECTION OF SPINAL CORD, SHOWING THE ASCENDING TRACTS ON THE RIGHT SIDE, AND THE DESCENDING ON THE LEFT.

C.P., crossed pyramidal; *R.S.*, rubro-spinal; *D.P.*, direct pyramidal; *O.S.*, olivo-spinal; *Low.*, tract of Loewenthal; *C.*, comma; *G.*, Goll; *B.*, Burdach; *D.C.*, direct cerebellar (Flechsig).

(*fasciculus cuneatus*) which goes to the nucleus cuneatus, and the tract of **Lissauer** (marginal tract), composed of relatively short processes running upwards for a few segments above their point of entry. The tracts of Goll and of Burdach are concerned with conscious sensation, of Lissauer with reflex function.

The chief **endogenous** ascending tracts are the tract of Gowers and the direct cerebellar tract. **Gowers' tract** (antero-lateral ascending) is a *composite* tract which contains fibres from the dorsal horn cells of the *opposite* side, and from Clarke's column of cells on

the *same* side. Some of the former go to the optic thalamus and some to the inferior corpora quadrigemina. The fibres from Clarke's column constitute the *ventro-spino-cerebellar* tract, and they proceed to the cerebellum via the superior peduncle. The **direct cerebellar tract** (Flechsig, *dorso-spino-cerebellar*) is composed of fibres from Clarke's column on the same side. Its fibres proceed direct to the cerebellum via the restiform body. The position of these tracts is seen in Fig. 38.

THE DESCENDING TRACTS.—All the descending tracts are *endogenous* in origin. The most important are the **pyramidal** or cortico-spinal, the **rubro-spinal** or pre-pyramidal, and the **tract of Loewenthal.** Of these the pyramidal is the most important in man, being the only efferent path along which voluntary motor impulses can be sent. It takes origin from large cells, known as Betz cells, which lie in the pre-central convolution of the cerebral cortex. In the medulla oblongata the greater number of the fibres of this tract cross to the opposite side, forming the **crossed pyramidal tract,** while the remaining fibres run downwards, without crossing, as the **direct pyramidal tract.** The fibres of the crossed pyramidal tract end by synapsing with cells of the dorsal horn of grey matter. These dorsal horn cells are intermediary, and convey the impulses to the motor cells in the ventral horn. The fibres of the *direct* pyramidal tract eventually cross in the ventral white commissure, and by the mid-thoracic region none are left. They synapse with the ventral horn cells. The pyramidal tract is the great motor tract of the cord; it contains about 80,000 fibres on either side in the cervical region. Destruction of the Betz cells, from which these fibres arise, or injury to the tract itself, causes complete paralysis of voluntary movement in man. In many lower animals, however, such injury is not followed by paralysis; there must therefore be some other pathway by which motor impulses are conveyed from brain to cord, and probably the most important is the **tract of Loewenthal,** the function of which in man is co-ordinative. This tract is composed of fibres

from the thalamus and the superior corpora quadrigemina of the opposite side, and of fibres from the olivary and vestibular nuclei of the same side. These are distributed to the ventral horn cells.

The **rubro-spinal tract** is also a motor tract, its fibres taking origin in the red nucleus and being distributed to the motor cells in the grey matter. It is not under the control of the will, but is activated by impulses arising in the dentate nucleus of the cerebellum. This tract is relatively much more developed in animals than in man. A small descending tract, the **comma tract,** lying in the dorsal columns of white matter, consists of the descending branches of the dorsal root (sensory) fibres, and is distributed to the grey matter at the lower levels. It subserves reflex functions.

The Functions of the Cord.

The spinal cord subserves two great functions: (1) it serves both as a pathway for impulses travelling to and from the brain, and as a means of communication between the different segments of the cord; (2) it is involved in the performance of a number of important reflexes. In both cases it acts, as it were, mechanically, being in no sense a seat of consciousness.

The Spinal Cord as a Path of Conduction.—When the spinal cord of a mammal is divided in the upper cervical region, the animal quickly dies owing to paralysis of the great muscles involved in respiration. If the division be carried out in the lower cervical region —*i.e.*, below the origin of the phrenic nerve—the animal does not necessarily succumb; transections of the cord at lower levels are still less likely to be fatal. The area of the body innervated by the part below the seat of operation undergoes an immediate loss of movement and sensation. The tone of the bloodvessels innervated from regions below the section is temporarily abolished, returning after the lapse of a certain period. These effects are referable to interruption of nerve-tracts from important centres at higher levels. Respiratory paralysis is due to loss of communication between the motor nerve-cells of the respiratory

muscles and the respiration centre in the medulla oblongata. The loss of voluntary movement depends upon the interruption of paths conveying motor impulses from the brain, and so on.

By making partial lesions of the cord and by study of the effects of disease, one can determine the function of certain of the named tracts. Such experiments show at the same time that the path towards the brain of certain definite sensory impulses is not *entirely* along named tracts, but may in part be situated in the grey matter. By hemisection of the cord we are enabled also to determine whether the pathways cross the middle line within the cord or remain on the same side throughout. Thus it is known that the main *descending* motor path, and the *ascending* paths for the sensations of 'position' and of **tactile discrimination** (columns of Goll and Burdach) do not cross the middle line in the cord itself, whereas they do cross at a higher level. The fibres conveying the sensation of **heat** and **cold** and of **pain** travel upwards partly in the grey substance, and cross to the opposite side within the cord. Hemisection experiments also show the spino-cerebellar fibres in Gowers' and the direct cerebellar tracts (which are uncrossed), while not concerned with conscious sensation, are of considerable importance in the co-ordination of movement.

THE SPINAL CORD AS A REFLEX CENTRE.—In a previous part of the book (p. 37) we have already discussed reflex action. In the lower animals independent reflex activity of the cord is more pronounced than in higher animals. With increasing development of the brain the reflex functions of the cord gradually come to occupy a more subordinate position, and in man we can point only to a relatively small number of independent reflexes mediated by the cord. The mechanisms of micturition, defæcation, ejaculation, and parturition, with their centres in the lumbar region, as well as many tendon reflexes, are in man carried out apart from the brain. In lower mammals—*e.g.*, the dog or cat—these reflexes are present along with others which are of much interest. The hind-limb of a **spinal dog** (a dog with its cerebrum removed) can execute scratching move-

ments when a certain area of the skin, broadly speaking co-extensive with the side of the thorax and abdomen, is tickled. When the animal is lifted off the ground so that its lower limbs hang downwards, the mechanical stretching of the muscles and tendons produces a rhythmic alternate beat of the lower limbs, as in the act of walking. When a spinal cat is set upon its feet, the muscles ordinarily concerned with the maintenance of posture so act reflexly as to maintain the standing posture. In fact, it is now known that reflex tonus of muscles is confined only to those muscles concerned with the maintenance of posture or of directive function—*e.g.*, the eye muscles.

II. The Brain.

The brain consists of three main divisions—the **fore-brain** (comprising the two cerebral hemispheres with the basal ganglia), the **mid-brain**, and **hind-brain** (consisting of the cerebellum, pons, and medulla oblongata). With the progress of evolution the cerebral hemispheres become enormously developed relatively to the other parts. This relative preponderance of the cerebral hemispheres culminates in man, in whom the psychical activities of the central nervous system are most complex. The lower parts of the brain, which do not share in this excessive development, subserve functions of the highest importance, though not associated with consciousness. The student should refer to his text-book of anatomy for a description of the gross structure of the organ.

The Medulla Oblongata.—This important structure is obviously from its shape a modified portion of the spinal cord. Its internal structure is best studied by making sections at different levels. From below upwards we shall describe three such sections.

1. **Level of Pyramidal Decussation.**—As in the cord, the white matter is external, the grey matter, which encloses the central canal, internal. Owing to increasing development of the dorsal columns of white matter, the dorsal horns of grey matter become opened outwards so as to lie transversely, each horn swelling

out at the tip to form the **tubercle of Rolando,** the grey matter of which is part of the sensory nucleus of the fifth nerve. Just outside the tubercle of Rolando is a bundle of white fibres, the **descending root of the fifth nerve.** At this juncture it may be as well to state that the fibres of all sensory cranial nerves having cells

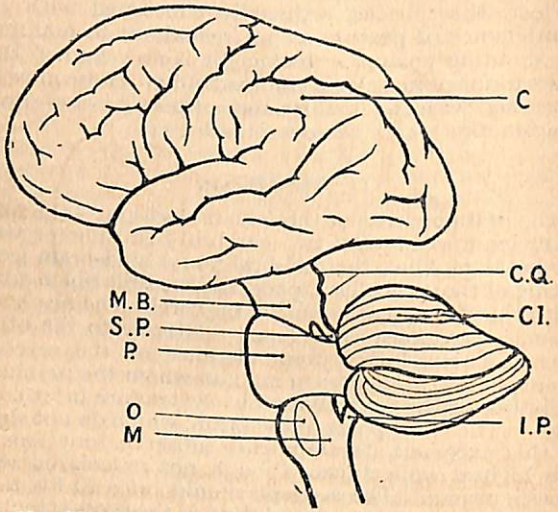


FIG. 39.—DIAGRAM OF ENCEPHALON, SHOWING ITS CHIEF PARTS.

C., Cerebrum; *Cl.*, cerebellum; *M.B.*, mid-brain; *P.*, pons; *M.*, medulla oblongata; *C.Q.*, corpora quadrigemina; *S.P.*, superior cerebellar peduncle; *I.P.*, inferior cerebellar peduncle (restiform body); *O.*, olive.

of origin in outlying ganglia end within the brain in the same fashion as the sensory nerve fibres within the cord —viz., by branching into two divisions, one ascending and one descending. In the case of the cranial sensory nerve fibres, however, the ascending branch is short, the descending one long. The white fibres applied to the outside of the tubercle of Rolando are the descend-

ing branches of the fifth nerve; they synapse round cells of the tubercle of Rolando, which therefore forms a sensory nucleus of the fifth.

In the open angle formed by the dorsal horns—*i.e.*, within the dorsal columns of white substance—two groups of nerve cells begin to appear and become more prominent at a still higher level. One group, the

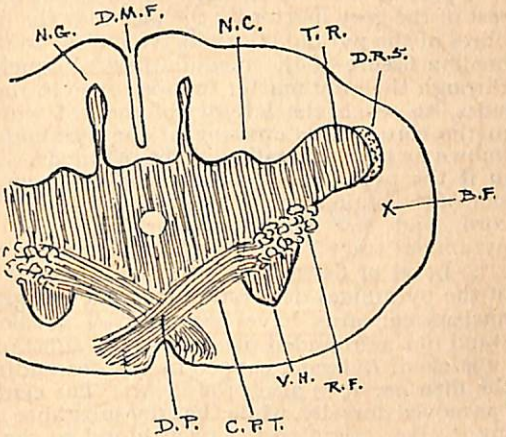


FIG. 40.—SECTION OF MEDULLA OBLONGATA AT LEVEL OF PYRAMIDAL DECUSSATION. (DIAGRAMMATIC.)

N.C., Nucleus cuneatus; *N.G.*, nucleus gracilis; *V.H.*, ventral horn; *D.P.*, decussation of the pyramids; *C.P.T.*, crossed pyramidal tract; *R.F.*, reticular formation; *T.R.*, tubercle of Rolando; *D.R.*5, descending root of fifth nerve; *D.M.F.*, dorsal median fissure; *B.F.*, bundle of Flechsig (direct cerebellar).

nucleus gracilis, lying within the column of Goll, is a *relay station* for the fibres of Goll's tract. The external group, the **nucleus cuneatus,** is similarly a relay station for the fibres of the tract of Burdach. The ascending branches of the spinal sensory nerve fibres therefore terminate by synapsing with the cells of these nuclei. New nerve fibres, springing from the nucleus gracilis and

nucleus cuneatus, cross the midline to form the tract of the **lemniscus, or fillet,** and convey the sensory impulses to the **optic thalamus,** whence the third (and last) neurone on the sensory tract transmits the impulses to the cerebral cortex. Associated with the dorsal region of this part of the medulla there are, therefore, three important sensory nuclei on each side

A part of the ventral horn becomes cut off from the rest of the grey matter by the fact that the descending fibres of the pyramidal tracts lying close to the ventral median fissure of the medulla pass obliquely inwards through the grey matter to cross over to the opposite sides, to reach the lateral columns of white matter in the cord. This crossing of the pyramidal tract is known as the **decussation of the pyramids.** By means of it the pyramidal fibres descending from the right side of the brain come to lie on the left side of the spinal cord, and *vice versa,* whence the name "crossed pyramidal tract."

2. **Level of Sensory Decussation.**—Above the level of the pyramidal decussation the nucleus gracilis and nucleus cuneatus have become well developed, and stand out as rounded masses of grey substance. The tubercle of Rolando, capped by the descending root of the fifth nerve, is also prominent. The central canal has moved dorsally, while the grey substance surrounding it gives origin to the twelfth and to the eleventh cranial nerves. The tract of the pyramids is anteriorly placed on each side of the ventral median fissure, now very shallow. Lateral to the pyramids is a swelling, the commencement of the **olive,** which projects on the side of the medulla. A wavy band of grey matter, the olivary nucleus, from which is derived the olivo-spinal descending tract of the cord, is situated within this projection. Dorsal to the olivary nucleus and laterally situated are the tracts of Gowers and of Flechsig, the fibres of which are on their way towards the cerebellum. The main grey substance occupying the interior of the medulla becomes broken up, by the passage of nerve fibres through it, into a well-marked **reticular formation,** whose origin has already been noted in the upper cervical region of the spinal cord.

This particular level of the medulla oblongata is especially characterised by a crossing of the ascending sensory fibres which proceed from the gracile and cuneate nuclei, the so-called **sensory decussation.** These nerve fibres dip ventrally, decussate in the mid line, and come to lie just dorsal to the tracts of the

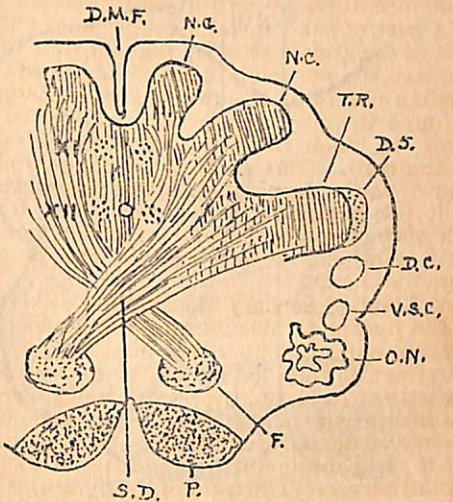


FIG. 41.—SECTION OF MEDULLA OBLONGATA AT LEVEL OF SENSORY DECUSSATION. (DIAGRAMMATIC.)

D.M.F., Dorsal median fissure; *N.G.*, nucleus gracilis; *N.C.*, nucleus cuneatus; *T.R.*, tubercle of Rolando; *D.5*, descending root of fifth nerve; *D.C.*, direct cerebellar tract; *V.S.C.*, ventro-spinal cerebellar tract (Gowers); *O.N.*, olivary nucleus; *P.*, pyramid; *F.*, fillet, or lemniscus; *S.D.*, sensory decussation.

pyramids. From their origin until they have crossed over they are known as the **internal arcuate fibres.** They are then continued upward as the **lemniscus,** or **fillet,** being joined on the way by other fibres from nuclei of the cranial sensory nerves, and end eventually in the **thalamus** at the base of the cerebrum.

We have now seen that the (descending) pyramidal fibres decussate in the lower part of the medulla, while the (ascending) sensory fibres of the dorsal columns of the cord form synapses on the *homolateral* side, and the

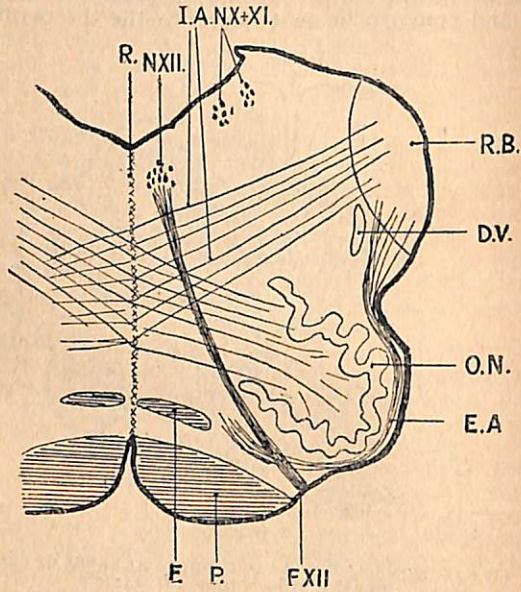


FIG. 42.—SECTION OF MEDULLA OBLONGATA AT LEVEL OF MID-OLIVE. (DIAGRAMMATIC.)

R., Raphe; *N.XII.*, nucleus of twelfth nerve; *I.A.*, internal arcuate fibres; *N. X. + XI.*, nuclei of tenth and eleventh nerves; *R.B.*, restiform body; *D.V.*, descending root of fifth nerve; *O.N.*, olivary nucleus; *E.A.*, external arcuate fibres; *F.XII.*, issuing fibres of twelfth nerve; *P.*, pyramid; *F.*, fillet.

sensory fibres from these cross at a level just above the pyramidal decussation. By these decussations the **left cerebral hemisphere** is brought into relation with the **right side of the cord,** and *vice versa*.

3. **Level of Mid-Olive.**—Here the central canal has opened out dorsally to form the fourth ventricle. In the floor of this lie part of the nucleus of the twelfth cranial nerve (mesially placed), the dorsal nucleus of the tenth (more laterally placed), and, still higher up, the dorsal nucleus of the ninth cranial nerve. The fibres of the twelfth nerve emerge from the ventral part of the medulla in the angle between the pyramids and the olivary body; those of the eleventh, tenth, and ninth in the angle between the olive and the inferior peduncle of the cerebellum (**restiform body**). Fibres are observed coming from the gracile and cuneate nuclei and curving round the *lateral* aspect of the olivary nucleus. These, the **external arcuate fibres,** join the restiform body of the same or of the opposite side. The fibres of the direct cerebellar tract (Flechsig), which are uncrossed, also enter the cerebellum by the restiform body. The nerve fibres of Gowers's tract do not enter the cerebellum by this route, but continue upwards through the pons, then curve backwards and enter by the superior cerebellar peduncle.

The fibres of the eighth cranial nerve, which come partly from the cochlea, in which is the organ of hearing (cochlear division), and partly from the semicircular canals, utricle and saccule (vestibular division), concerned with the function of equilibration, have sensory nuclei in this part of the medulla. From the vestibular nuclei (Deiters) are derived the vestibulo-spinal tracts, which are concerned in reflex maintenance of posture.

Functions of the Medulla Oblongata.—Besides acting as a bond of union between the spinal cord and higher parts of the brain, the medulla subserves certain reflex functions of the highest importance. Here are the **respiratory centre, vasomotor centre,** and **cardio-inhibitory centre.**

The remaining portion of the central nervous system can now be more conveniently described from the cerebrum downwards.

The Cerebral Hemispheres.

The grey matter of the cerebral hemispheres lies externally (**cerebral cortex**), being folded in complex fashion to obtain increased area. Underneath the cortex lies white substance (**corona radiata**), deep in the substance of which are buried great masses of grey matter (optic thalamus, caudate nucleus, and lenticular nucleus). The two hemispheres are united across the middle line by a mass of commissural fibres—the **corpus callosum**—and are connected to the lower parts of the central nervous system by the mid-brain.

Functions of the Cortex.

To the cortex belongs an entirely new function as compared with that of the spinal cord. In man it is the seat of consciousness, of thought, of memory, and of experience—in other words, of psychical processes. With the increase in size as we proceed from the lower animals to higher, these psychical activities become increasingly complex. Removal of the cerebral hemispheres in a frog produces little alteration in the behaviour of the animal, provided the corpora striata are left behind. Even when these are removed, the animal, on stimulation in different ways, can carry out very complicated reactions. In the absence of all external stimulation, however, it shows no spontaneous movements, sitting quite still in one spot until it dies. Even in this animal, the cerebral hemispheres are necessary for volitional impulses. A decerebrate pigeon can fly when thrown into the air, and can alight again on a perch, maintaining its equilibrium perfectly throughout. In the absence of stimulation it sits still as if asleep. When irritated, it defends itself, so also when a burning candle is brought close to its beak; but no matter how often it is burnt, it never learns to 'dread the fire.' In other words, it is incapable of profiting by experience, which fact indicates that educability by contact with the environment is a function of the cortex. Without the cerebral cortex there

is no memory. By successive partial operations, separated by considerable intervals of time, Goltz succeeded in removing the whole cerebral cortex of a dog without fatal result. Previous to the operation the animal had been taught to 'give its paw.' After the operation this acquired trick was impossible as the animal had lost all its mentality. It was extremely restless, and, except when it was asleep, spent its time in continual restless movement. It responded to stimulation, growling and biting when touched; it never learnt to recognise its feeding-times, and showed no sign of pleasure when caressed or of fear when threatened. These experiments show that while memory, intelligence, and emotion are blotted out with removal of the cortex, the power of carrying out, under suitable stimulation, highly co-ordinated movements may still remain.

LOCALISATION OF FUNCTION IN THE CORTEX.—For a long time it was thought that no part of the cortex is developed for one particular function. Broca (1861), however, showed paralysis of speech to be due to injury or under-development of a certain area of the cortex. Dr. Hughlings Jackson (1864) also noted that in certain forms of epilepsy the twitchings begin first in some definite part—*e.g.*, the fingers—spreading thence up to the shoulder; he associated this condition with injury to a definite area of the brain. Fritsch and Hitzig in 1870, stimulating definite parts of the brain of a dog with faradic shocks, elicited definite movements of the body.

These areas, associated with voluntary movement, have been termed **motor areas.** In man they lie in the precentral convolution of the frontal lobe. The movement produced by stimulation of these parts of the cortex are on the **opposite side** of the body from that stimulated, and are co-ordinated, the corresponding muscles acting not individually, but in groups, the tone of antagonists, where tone is present, being simultaneously inhibited. In other words, the representation of the muscles in the cortex is physiological; only in the clusters of the nerve-cells in the ventral horn of the spinal cord do we find any approach

to anatomical representation of the muscles. Each individual part of the motor region presides over its own particular movement, and we can map out the whole area into provinces corresponding to lower limb, trunk, arm, head, and neck, these in turn being subdivided into smaller areas corresponding to particular movements of the larger divisions of the body.

Irremediable injury to these areas in man produces permanent paralysis of voluntary movement on the opposite side of the body. In some animals, such as the cat or the sheep, the motor area may be removed and no paralysis ensue. In higher animals, such as the monkey, there is a temporary paralysis, which may largely be recovered from. With advancing evolution the functional activity of the neuro-muscular mechanism becomes more and more bound up with this particular region of the cortex.

Other areas of the brain, known as **sensory areas,** are concerned with sensation. The **visual area** is a fairly large region, localised in the occipital lobe. Stimulation of this region produces a conjugate movement of the eyes to the opposite side. That it is not a motor region is known from excision of the part, which is followed by no corresponding paralysis of movement, but by a peculiar form of blindness involving the homolateral half of each retina, the central part, or fovea centralis, of each eye being, however, bilaterally represented (see later, p. 236). The **olfactory area** is situated in the hippocampal convolution, in which part **gustatory** sensations are also perhaps experienced. The **auditory area** lies in the superior temporal lobe. Stimulation of this area in a monkey causes the head to be turned to the opposite side and the ears to be pricked. Unilateral ablation of the area causes partial deafness on both sides; entire ablation of the cortex of both temporal lobes causes complete deafness. In no case is there interference with voluntary movement. It is probable that **tactile and muscular sense** are localised in the post-central convolution of the parietal lobe.

When the foregoing regions of the cortex are

excluded, there still remain large areas stimulation of which evokes no visible response. Such areas, very extensive in the human brain, are known as **association areas,** and are linked up in complex fashion by white fibres (association fibres) with the motor and sensory regions. There are three great association areas: anterior (or prefrontal), middle (in the island of Reil), and posterior (parieto-temporal). These areas are concerned in intellectual and emotional processes, and in inhibition; damage to any part of them leaves the individual mentally different from before, and with less power of inhibitory control.

The power of **speech,** which belongs only to man, is a result of the higher evolution of the brain. The fact that a child commences to speak only after it has learned to handle objects and to walk, is an indication of the complexity of this function. The loss of 'intelligent' speech is called **aphasia.** It is an exceedingly common symptom in disease of the brain, and yielded the first evidence of cerebral localisation. It has also been demonstrated that the distribution of areas concerned in the interpretation or production of language is very wide. The function is not localised in both hemispheres, but only in one. A right-handed person controls his speech with his left hemisphere and *vice versa*. In cases of damage to the hemisphere that controls speech, it has been shown that in some cases the other hemisphere is capable of taking over the function. This almost invariably occurs in children, but is rarer with adults. It is to be noted that pure aphasia does not imply any paralysis of the muscles concerned with writing or articulation. Such paralysis may occur, however, at the same time as aphasia, owing to the lesion involving the motor centres for the muscles concerned in addition to the centres for speech.

The production of spoken or written words is in the immediate sense a purely *motor* function; the interpretation of such language involves in the first instance a *sensory* mechanism. We find, indeed, that aphasia may be (*a*) 'motor,' in which the power of articulating or writing words is lost, although the patient can still

produce meaningless sounds, as the peripheral neuro-muscular mechanism is still intact; or (*b*) 'sensory,' in which there is inability to comprehend spoken or written language, although the patient can still hear sounds and see objects. In other words, the parts of the brain involved in aphasia are not simply the visual and auditory centres, or the motor centres controlling the muscles employed to produce speech.

Sensory aphasia implies either word-deafness or word-blindness. In **word-deafness** spoken words are heard as unintelligible sounds; to the patient they have no meaning. Similarly in **word-blindness** the symbols on a printed page, while seen, convey as much meaning as a page of Chinese to an ordinary European.

The existence of such defects, which may be suddenly produced by a lesion of the brain, throws an interesting light on the function of some of the association centres. It is believed that close to the visual and auditory *sensory* areas there are regions of the cortex in which the memories of certain particular stimuli with their connotation are pigeon-holed, as it were. These are known respectively as the **visio-psychic** and the **audito-psychic** areas. When these parts are damaged, all the training and experience attaching thereto are blotted out. The meaning of words, whether spoken or written, as the case may be, is impaired. It will now be plain why a sensory aphasia implies a corresponding inability to produce rational language; when a definite connotation no longer attaches to words, the production of intelligible language is impossible. Sensory aphasia, and especially word-deafness, is always associated with some degree of mental deficiency.

In cases of motor aphasia there may be no loss of intelligence. From the existence of these cases it is concluded that individual portions of the cortex, connected by association fibres with the areas for interpretation of language, store the muscular 'direction' impressions that have been acquired during the process of learning to speak and to write. When these areas are damaged the individual can still speak or write, but he cannot utter the words which he wishes.

Reference has already been made to Broca's original discovery of a 'speech centre,' which he localised near the inferior part of the precentral convolution. It is now generally held, however, that the control of speech is not invested in such a localised area of the cortex, but is more probably a function involving the co-operation of widespread cortical and sub-cortical areas in the brain.

STRUCTURE OF THE CEREBRAL CORTEX.—The cerebral cortex contains a large number of nerve cells which are of varying size, and as a rule of pyramidal shape, the apex of each pyramid pointing towards the surface. The axons arise from the basal part of the cells, and in many cases are directed inwards; many dendrites spring from the sides of these pyramidal cells, while the apical part of each ends as a dendrite. The cells are obviously arranged in strata, but to such an extent does one stratum merge with another that different authorities have described different numbers of layers. Following Brodmann and Vogt, whose classification is based on a study of the development of the cortex, we may distinguish six layers, named as follows from the surface inwards:

1. The **outer molecular layer,** containing many nerve fibres and some horizontally placed nerve cells, and neuroglial cells.
2. The **external granule layer,** containing small, round and pyramidal cells.
3. The **outer pyramidal cell layer,** composed of large pyramidal cells.
4. The **inner granule layer,** or granular layer, containing closely packed stellate nerve cells.
5. The **inner pyramidal layer,** containing large and frequently solitary nerve cells.
6. The **inner cell layer,** containing polymorphic cells.

There are thus five cell layers and one fibre layer. Of the cell layers the inner develops first, then the middle, and finally the outer, the great depth of which is especially characteristic of the brain of man.

The different regions of the cortex vary in respect to the degree of development of these different layers. The motor region is especially characterised by the

existence of large pyramidal cells (**Betz cells**) in the inner pyramidal layer; from these the fibres of the pyramidal tract take origin. In the visual area the lamination is very conspicuous, the inner granule layer being especially prominent. Comparative study makes it probable that the external granule layer subserves the higher psychic or associational functions of the brain, that the inner granule layer is concerned with the reception of afferent impressions from the lower sensory neurones or from other parts of the cortex, and that the inner cell layer subserves the lower voluntary and instinctive activities of the organism.

White Matter of Cerebrum.—The nerve fibres of the white matter are of three kinds—namely, projection fibres, association fibres, and commissural fibres. The **projection fibres,** which are either *afferent* or *efferent,* connect the cerebral cortex with the grey matter in lower parts of the central nervous system. The **association fibres** join together different parts of the cortex on the same side. The **commissural fibres,** which cross in the corpus callosum, connect portions of the right cortex with portions of the left. A study of the time of myelination of these different systems shows that the afferent projection fibres develop first, and certain of the association fibres last.

The main afferent projection fibres come from the thalamus, whence they spread to all parts of the cortex as **thalamo-cortical** fibres. The main efferent projection fibres are: (1) the **pyramidal** fibres from the Betz cells of the motor area; converging as they pass downwards, they form the tract of the pyramid; (2) the **cortico-pontine** fibres (from frontal and temporal lobes), which descend by much the same route as the pyramidal fibres, ending, however, in the pons. They form the first relay of the cortico-ponto-cerebellar tract.

The Internal Capsule.—At the base of the brain are found certain masses of grey matter, which function as afferent and efferent centres of a lower level. Situated among these centres is the **internal capsule,** a band of white matter, which conveys downwards

in its middle portion the pyramidal fibres from the motor region of the cortex and the cortico-pontine fibres from the frontal and temporal lobes. When hæmorrhage occurs into this part, a motor paralysis of the opposite side of the body results. The anterior and posterior portions of the internal capsule consist of fibres conveying sensory impulses to the cerebral cortex.

THE BASAL GANGLIA. — These consist of certain large masses of grey matter situated at the base of the brain in the substance of the cerebral hemispheres. They represent the remains of the higher centres in the lower animals. In man, the functions of these centres have been taken over mainly by the cerebral cortex. The basal ganglia are most conveniently divided into two groups:

1. The Optic Thalamus.
2. The Corpus Striatum, composed of the Caudate and Lentiform Nuclei.

The **optic thalamus** serves as the main and the last relay station of the conscious sensory tracts passing to the cerebral hemispheres. It is here that the final neurone arises before passing to the cortex. The thalamus also serves as a reflex centre and it is believed to be concerned with many emotional reflexes (*e.g.*, rage). The thalamus also functions as a 'crude' receptor of sensation. It has been shown that if, as in the treatment of gunshot wounds, the cerebral cortex be removed and the thalamus be left intact, the interpretation of the various sensations received by the body will be of a gross nature. The individual is totally unable to differentiate the degree of his sensations. He feels either severe pain or great pleasure. Similarly he can feel that an object is either hot or cold, but he cannot appreciate variations in the temperature. As a result of this extremely crude interpretation, each stimulus, no matter how slight, is apt to be accompanied by severe emotional disturbance.

Efferent fibres pass from the thalamus to the cortex, as noted above, and also to the **corpus striatum** which is concerned with motor function, also in a crude

manner. The **lentiform nucleus** consists of two parts: (1) the **globus pallidus** or medial portion, composed of large, multipolar cells similar to those of the motor part of the cortex; and (2) the **putamen** or lateral segment which, together with the **caudate nucleus**, is composed of small cells similar to those of the sensory part of the cortex. The efferent impulses of the corpus striatum apparently arise entirely from the globus pallidus. The efferent fibres run almost entirely to the red nucleus, substantia nigra and pontine nuclei, whence arise the various extra-pyramidal tracts (vestibulo-spinal, ponto-spinal, rubro-spinal, etc.). The stimuli to the corpus striatum appear to come solely from the optic thalamus. The functions of the corpus striatum are rather vague, but it is probable that the impulses which descend from the motor region of the cortex are *steadied* by additional impulses originating in this ganglion. If it is damaged, various disturbances in motor power occur. These consist of rigidity, tremor and lack of precision in movements, and it is suggested that the corpus striatum serves to dampen down the influence of the lower centres, which make themselves manifest if it is damaged. This occurs clinically in cases of paralysis agitans (fine tremor) and of athetosis (coarse tremor).

THE MID-BRAIN.—On the ventral aspect of the mid-brain are the two cerebral peduncles, appearing to external view as rope-like strands, which converge from their origin in the cerebral hemispheres to enter the pons almost side by side. The cerebral peduncles contain on the ventral aspect the pyramidal and cortico-pontine fibres (motor), and, more dorsally placed, the afferent sensory fibres running to lower parts of the thalamus. On the dorsal aspect of the mid-brain are the quadrigeminal bodies. Embedded in the substance are certain important nuclei of grey matter, especially the oculo-motor, trochlear, and red nuclei. The position of these various parts is shown in the diagram. The crusta, or **basis**, of the cerebral peduncle, conveying the pyramidal and cortico-pontine fibres, is separated from the more

dorsal part, the **tegmentum,** by **substantia nigra.** The main ascending sensory tract lies in the tegmentum as the lateral fillet, or **medial lemniscus,** and ends in the thalamus. The reflex centre for contraction of the pupil, associated with the oculo-motor nucleus, is in the mid-brain. The **red nucleus** receives fibres from the basal motor ganglia (globus pallidus) of

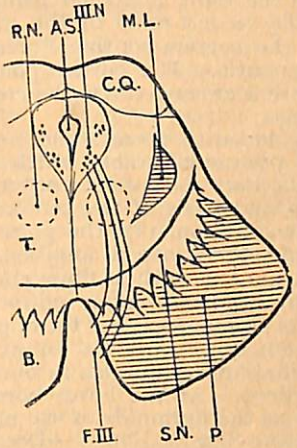


FIG. 43.—SECTION OF MID-BRAIN. (DIAGRAMMATIC.)

B., Basis cerebri; *T.*, tegmentum; *C.Q.*, one of the corpora quadrigemina; *A.S.*, aqueduct of Sylvius; *III.N.*, third nucleus; *M.L.*, medial lemniscus; *P.*, pyramidal and cortico-pontine fibres; *S.N.*, substantia nigra; *F.III.*, fibres of third or oculo-motor nerve; *R.N.*, red nucleus.

the cerebrum of the same side, and from the cerebellum of the opposite side. It gives origin to the **rubro-spinal tract,** which crosses to the opposite side in the mid-brain, and ultimately in the spinal cord is found ventral to the pyramidal tract and is thus sometimes called the *pre-pyramidal* tract.

THE PONS.—A great band of transverse fibres, the middle cerebellar peduncles, crosses the ventral aspect

of the pons. This, however, is not a complete transverse band, connecting the right cerebellar hemisphere with the left. The nerve fibres of which it is composed take origin on each side not far from the middle line from scattered nerve cells, the **nuclei pontis.** The fibres from the right side cross the middle line and go to the left cerebellar hemisphere; those from the left side to the right cerebellar hemisphere. These fibres form the second relay of the cortico-ponto-cerebellar tract, the cortico-pontine fibres synapsing with the nuclei pontis. The cortico-ponto-cerebellar tract is therefore a crossed tract, the crossing taking place in the pons.

Just dorsal to these transverse fibres lie the fibres of the pyramidal tract, which we have now traced from the Betz cells of the cortex, through the internal capsule and basis of the cerebral peduncles, to their present situation. In the pons the pyramidal fibres are aggregated into a number of separate bundles. A large number of these fibres end in the pons by forming connections, direct or indirect, with certain motor nuclei of cranial nerves of the opposite side. From the mid-brain downwards as far as the spinal cord the pyramidal fibres diminish in number by forming such connections. At the lower border of the pons they appear as the pyramids of the medulla oblongata.

Cerebro-Spinal Fluid.—Deep in the substance of the brain are cavities known as **ventricles.** These are in communication with one another and with the central canal in the cord. All these cavities are filled with a fluid called the cerebro-spinal fluid. This fluid is secreted by the *choroid plexuses*, which are tufts of capillary bloodvessels found in the ventricles.

Cerebro-spinal fluid is a modified form of lymph, and in the adult it amounts to about 120 c.c. It is colourless and has a specific gravity of 1·005. It contains but little protein (0·02 per cent.), and it does not clot. The diffusible constituents of the blood plasma, notably glucose and urea, are found present in the cerebro-spinal fluid in the same concentration as in the blood. A few lymphocytes are usually present, but under normal conditions there are *no granular*

leucocytes. The former are increased in general paralysis of the insane, and the latter are present in large numbers in acute cerebro-spinal meningitis. Cerebro-spinal fluid is often removed by lumbar puncture for diagnostic purposes, and to relieve intracranial pressure in hydrocephalus.

The Cerebellum.

This organ, which is united to other parts of the brain by the cerebellar peduncles—superior, middle, and inferior—consists of a central or vermiform lobe and of two lateral lobes. The grey matter, which lies externally, is sharply divided into two distinct layers—an outer or **molecular layer,** and an inner or **granular layer.** Between these two is situated a single incomplete stratum of large nerve cells, **Purkinje cells.** Embedded in the white matter are certain grey nuclei, of which the **nucleus dentatus**—a wavy lamina found in each lateral lobe—is the largest.

The flask-shaped Purkinje cells are the great efferent cells of the cerebellum. The axon of each of these cells penetrates the granular layer and the white matter, ending in the *nucleus dentatus*, whence by a new relay the impulses are conveyed to the red nucleus of the mid-brain on the opposite side. On its superficial aspect each Purkinje cell forms an enormously rich ramification of dendritic processes which spread in the molecular layer. The cells of the granular layer are small and rounded with little cytoplasm and short dendrites. Their axons pass into the molecular layer, where each undergoes a T-shaped branching, the subdivisions running parallel to the surface of the grey matter. Whether they synapse with the cells of the molecular layer or directly with the dendrites of the Purkinje cells is not known. The cells of the molecular layer are known as basket cells, because their efferent axons form basket-like synapses around the bodies of the Purkinje cells.

Reference has already been made to **afferent fibres** from various sources entering the cerebellum. The tract of Flechsig, fibres from the olivary nucleus, and fibres

from the nucleus gracilis and nucleus cuneatus, reach the organ by the inferior peduncle; by the middle peduncle the ponto-cerebellar fibres enter, while the tract of Gowers enters by the superior peduncle. From whatever source these afferent fibres come, they end in one or other of two ways. Some (**moss fibres**) synapse with the granule cells, thus forming an indirect connexion with the Purkinje cells; others (**tendril fibres**) synapse directly with the dendrites of the Purkinje cells. The moss fibres thus form part of a long reflex arc involving the granular cells and, presumably, the basket cells, while the reflex path by the tendril fibres is shorter. **Efferent fibres** leave the cerebellum by all three peduncles, those in the middle peduncle crossing to the cerebellum on the opposite side. Fibres from the *nucleus fastigius* leave in the inferior peduncle to enter the nuclei of Bechterew and Deiter of the same side, and the olives of both sides. The superior peduncles carry fibres from all nuclei *except* fastigius to the red nucleus and optic thalamus of the opposite side.

Functions of the Cerebellum.—These have been studied by the same methods as are used to investigate the function of the cerebral cortex—viz., (1) excitation, (2) ablation, and (3) observation of cases in which the organ is diseased. While movements have been recorded as the result of **electrical excitation,** it is doubtful if these are not due to spread of the current to neighbouring parts of pons and medulla. In any case, there is no localisation of function as in the cortex cerebri, a result that is confirmed by the method of ablation. **Unilateral ablation** causes muscular weakness on the same side, the animal falling towards the affected side and sometimes continuing to roll over and over in the same direction; the eyes are affected with nystagmus. Considerable recovery occurs in a few days, though willed movements tend to be accompanied with tremor. After ablation of the whole cerebellum, this ' intention tremor ' is still more marked, and the time taken for recovery is still longer. The senses and the intellect are, however, unaffected, whence it is apparent that the cerebellum is not concerned in psychical processes.

In spite of its rich supply of afferent fibres *it is not concerned with conscious sensation.* When the cerebellum is diseased in *man*, the gait is reeling, the speech is halting, and the eyes are affected with nystagmus. The derangement is entirely neuro-muscular, the *intellect* being unaffected. The only sensory disturbance is a subjective feeling of giddiness, which in some cases is so severe as to cause the patient to roll over and over.

It is concluded that the cerebellum, by reflex processes that lie below the level of consciousness, controls and harmonises the action of the voluntary neuro-muscular mechanism. These reflexes, which depend largely upon afferent messages derived from muscles, tendons and joints, are known as **proprioceptive reflexes.**

Tracts and their Connections.

The more important tracts in the cord having been referred to, and the intercommunications between the different segments of the brain and these tracts having been described, it will be found profitable to study Fig. 44, with the help of the table on page 208.

It should be noted that the pyramidal fibres proceeding from the cerebrum to the grey matter in the cord constitute the **upper motor neurones.** The fibres which leave the ventral horn cells to supply the muscles are called the **lower motor neurones.** The former exercise a restraining influence upon the spinal reflexes, and where they are destroyed not only is there loss of voluntary control of the muscles they supply, but these pass into a condition of contraction known as **spastic paralysis.** Destruction of the *lower* motor neuron, however, in virtue of all motor impulses being cut off from the muscles, gives not only loss of control but also *loss of tone.* This is known as **flaccid paralysis.**

TABLE OF THE PRINCIPAL NERVE PATHS IN THE CENTRAL NERVOUS SYSTEM.

(See Fig. 44.)

No.	*Name.*	*Origin.*	*Destination.*	*Function.*
		EFFERENT.		
1.	Direct pyramidal	Cerebral cortex	Grey matter in cord	Motor.
2.	Crossed pyramidal	Cerebral cortex	Grey matter in cord	Motor.
3.	Rubro-spinal	Red nucleus	Grey matter in cord	Motor.
	All the above, usually by means of an intermediate neurone, stimulate the ventral horn cells, the axons of which supply the skeletal muscles.			
4.	Cerebello-cerebral (*a*) (*b*)	Cerebellum Cerebellum	Red nucleus Cerebrum via thalamus	Motor. Co-ordination.
5.	Cortico-ponto-cerebellar	Cerebral cortex Nucleus pontis	Nucleus pontis Cerebellum	} Co-ordination.

AFFERENT.

UNCROSSED.

6.	Direct cerebellar	Clarke's column	Cerebellum	Afferent stimuli to co-ordinate muscles of balance and locomotion.
7.	Ventro-spino-cerebellar	Clarke's column	Cerebellum	

Both the above tracts convey proprioceptive impulses from tendons, joints and muscles.

CROSSED.

8.	Burdach	Skin, etc. Nucleus cuneatus	Nucleus cuneatus Optic thalamus	Touch.
8*a*.	Goll	Skin, etc. Nucleus gracilis	Nucleus gracilis Optic thalamus	Touch.
9.	Spino-thalamic	Skin, etc. Dorsal horn cells	Dorsal horn cells Optic thalamus	Touch, pain, heat and cold.
10.	Thalamo-cortical	Optic thalamus	Cerebral cortex	Last relay for all conscious sensations, including paths 8, 8*a* and 9.

Note that 8 and 8*a* cross *en masse* in the *medulla*, whereas 9 crosses in clusters in the *cord*.

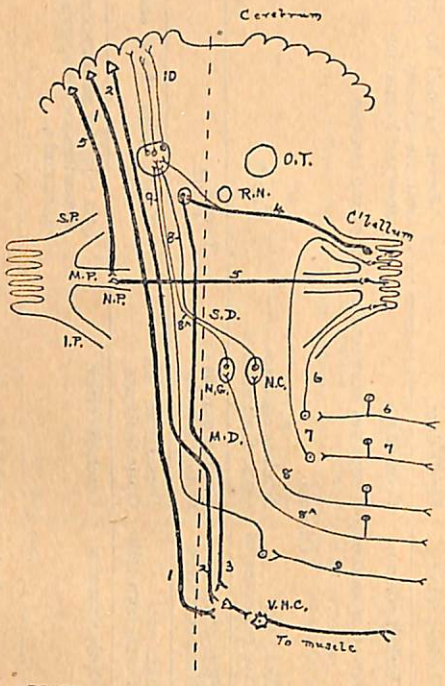


FIG. 44.—DIAGRAMMATIC SKETCH OF THE PRINCIPAL NERVE PATHS IN THE CENTRAL NERVOUS SYSTEM.

The *efferent* paths are shown in HEAVY, the *afferent* paths in LIGHT lines.

O.T., optic thalamus; *R.N.*, red nucleus; *S.P.*, *M.P.*, *I.P.*, superior, middle and inferior peduncles; *N.P.*, nucleus pontis; *S.D.*, sensory decussation (internal arcuate fibres); *N.G.*, nucleus gracilis; *N.C.*, nucleus cuneatus; *M.D.*, motor decussation; *V.H.C.*, ventral horn cell.

For explanation of the numerals, see Table, page 208.

III. The Autonomic Nerves.

There are two main sets of *efferent* nerve fibres found in the body. One of these may be said to be, in a restricted sense, under the control of the will. Its fibres convey the motor impulses to the skeletal muscles. The other set, which is involuntary in its action, is concerned with the innervation of the viscera—intestines, bloodvessels, glands and plain muscle generally. There are certain anatomical differences between these two sets of nerves, the most outstanding being the site of origin of the final neurone on the efferent path. The last relay in all the *voluntary* nerves commences in the ventral horn cells in the grey matter of the cord, whereas the final neurone of the involuntary nerves invariably arises at some point outside the cord. These involuntary nerves, most of which control functions essential for life, possess a certain power of self-government or autonomy, and this led Langley to name them the **autonomic nerves.**

The junction between two or more neurones is known as a **synapse.** When a number of such synapses occur at one spot, the swelling or structure formed is called a **ganglion.** It will be seen, therefore, that all the *autonomic nerves* have synapses or ganglia somewhere in their journey from the cord to their destination. Those fibres which are proceeding to, but have not yet reached, their *synapse*, are known as **pre-ganglionic** fibres. Those fibres which arise at the synapse, and which therefore constitute the final neurones, are called **post-ganglionic** fibres. All the pre-ganglionic fibres are *medullated*, and most of the post-ganglionic fibres are *non-medullated*.

It has been found convenient on anatomical and functional grounds to subdivide the autonomic nerves into two main divisions, those emerging in the thoracico-lumbar region, called the *sympathetic* nerves, and those arising in the cranial and sacral regions, named the *parasympathetic* nerves.

The **sympathetic nerves** have their ganglia arranged in two chains, one on each side of the vertebral

column, and, in addition, collateral ganglia not far removed. There are usually three ganglia in the cervical portion of the chain, eleven in the thoracic, four in the lumbar and four in the sacral region, together with the cœliac, mesenteric and renal ganglia in the abdominal cavity.

The pre-ganglionic neurones in the sympathetic nerves arise from the *intermedio-lateral column* of cells in the grey matter of the cord, and they all emerge in the ventral roots of the spinal nerves from the first thoracic to the third lumbar segments. Three possibilities may occur: these neurons may (*a*) pass to the nearest ganglion and there synapse with the final neurone; (*b*) pass *through* this and one or more ganglia in the chain and *then* synapse with the final neurone; or (*c*) pass through one or more of the ganglia without synapsing, and finally proceed to a collateral ganglion, there to synapse with the peripheral neurone. In the case of (*a*) and (*b*), the post-ganglionic fibres usually proceed to the mixed spinal nerves, to be distributed by them throughout the body. In the case of (*c*) they are distributed direct to the blood-vessels and viscera in the abdominal and pelvic regions.

The fibres which leave the spinal nerve to reach the adjacent ganglion are medullated, and this 'communicating arm' exhibits a white appearance, hence the name **white ramus communicans.** The *post-ganglionic* fibres which proceed to the spinal nerves are non-medullated, and collectively possess a grey appearance, thus giving origin to the name **grey ramus communicans.**

It must be clearly understood that, although the sympathetic chain of ganglia extends from the cervical to the sacral regions, *all* the sympathetic fibres emerge in the spinal nerves from the first thoracic to the third lumbar segments. Therefore, *all* the pre-ganglionic sympathetic fibres in the cervical and sacral portions of the chain must have arisen from the above region. It thus follows that there are no *white* rami communicantes in the cervical and sacral regions, although each ganglion

has one or more *grey* rami communicantes linking it up with the cervical and sacral nerves.

The **splanchnic nerves** are composed of masses of *pre-ganglionic* fibres which, emerging from the sympathetic chain, enter the abdominal collateral ganglia, there to synapse with the terminal neurones. The sympathetic nerves subserve many functions, to some of which reference has already been made. They convey vaso-constrictor impulses to the arterioles, accelerator and augmentor fibres to the heart, secretory fibres to the sweat glands, motor to the arrectores pili muscles and the dilator pupillæ fibres in the iris. They *inhibit* the musculature of the bronchioles and the whole length of the alimentary canal and that of the bladder wall, although they are *motor* to the pyloric and ileo-colic sphincters, and to the internal sphincter of the bladder.

The pre-ganglionic fibres of the **parasympathetic nerves** emerge from the central nervous system in the cranial and the sacral regions. In the former they are found in the third, seventh, ninth, tenth, and eleventh cranial nerves; and in the sacral region they emerge in the ventral roots of the second, third, and fourth nerves, forming the *nervi erigentes*. The parasympathetic nerves differ from the sympathetic in that their ganglia are usually found near, and frequently in the wall of, the organ which they supply. Many organs are supplied by both sympathetic and parasympathetic nerves, and when this is so these nerves are antagonistic to each other. This is well illustrated in the case of the heart, where the parasympathetic fibres in the vagus are inhibitory, and the sympathetic augmentory. The parasympathetic system contains vaso-dilators to the arterioles, secretory fibres to the salivary, gastric and pancreatic glands, and motor fibres to the bronchioles and the whole length of the alimentary tract, except the pyloric and the ileo-colic sphincters. Other functions mediated by the parasympathetic nerves are referred to when discussing the specific organs.

In addition to the parasympathetic nerves referred to above, there is reason to believe that similar

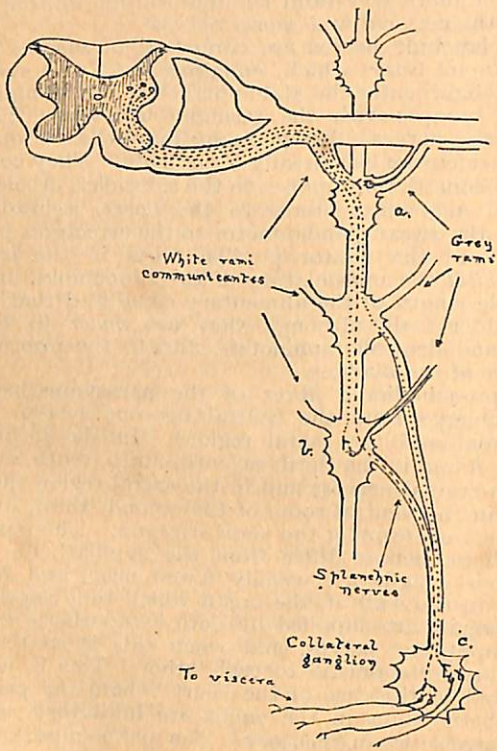


FIG. 45.—TO SHOW THE CONNECTIONS OF THE SYMPATHETIC FIBRES WITH THE GANGLIONIC CHAIN.

Broken lines indicate pre-ganglionic fibres; solid lines indicate post-ganglionic fibres; *a*, *b*, *c*, the different kinds of synapses referred to in the text.

efferent fibres are present in the *dorsal* roots of all the spinal nerves.

All the autonomic nerves have afferent as well as efferent fibres. These follow the usual course of afferent fibres when they enter the cord, and they give off collateral branches to the segment of the cord in which they end. In 'painful' conditions of certain viscera the pain is not felt in the viscera, but is referred to the skin in other parts of the body innervated from the same spinal segment as that to which the afferent sympathetic fibres enter. This is known as **referred pain.** In the wall of the intestine are the two plexuses of Auerbach and Meissner, and to these Langley gave the name **enteric autonomics.**

Action of Drugs.—The two systems of autonomic nerves act differently in their response to drugs. **Adrenaline** has an effect similar to stimulation of the entire sympathetic nervous system, with the exception that it does not cause a secretion of sweat. Its action is upon the myo-neural junctions. It has no action on the parasympathetics. **Ergotoxine** paralyses the *motor* fibres in the sympathetic nerves. **Pilocarpine** and **acetyl-choline** give an effect similar to stimulation of the parasympathetics, and they also stimulate the production of sweat. **Atropine** abolishes the effects arising from the stimulation of the parasympathetic nerves. This may be readily demonstrated experimentally in the inhibitory fibres to the heart, and in the secretory fibres to the salivary glands. It has no effect upon the vaso-dilator fibres supplying the salivary glands. **Nicotine** acts upon the synapses in the ganglia of both sets of autonomic nerves. In low concentration it acts as an excitant, in higher concentration it paralyses the synapses and prevents nerve impulses from passing. It has no effect upon the actual nerve fibres.

Chemical Nature of the Stimulus.—It was shown that when the parasympathetic fibres to the heart were stimulated, acetyl-choline, or a substance strongly resembling it, was liberated. Subsequent investigations have indicated that this is a feature of the parasympathetic nerves generally. In a similar

manner it has been demonstrated that when sympathetic nerves are stimulated, there is liberated in the organ supplied a substance resembling adrenaline. The evidence suggests that this substance is not actually adrenaline but something physiologically akin to it, to which the name **sympathin** has been given. It is concluded that it is a liberation of these substances which produces the results which follow the stimulation of these nerves. Accordingly it has been suggested that the parasympathetic nerves should be called **cholinergic,** and the sympathetic **adrenergic,** and that they should be thus classified. Whilst the post-ganglionic fibres of the parasympathetics are cholinergic, so also are the *pre*-ganglionic fibres of *all the autonomic nerves*. The post-ganglionic fibres of the sympathetics, however, whilst being in general adrenergic, contain one or two exceptions to this rule. Curiously enough, the sympathetic fibres to the adrenal glands form one of these exceptions: they are cholinergic.

CHAPTER XV

THE SENSES AND SENSE ORGANS—TOUCH, COMMON SENSATION—SMELL—TASTE

The Senses and Sense Organs.

An individual is enabled to become aware of what is going on around him by the fact that his brain receives certain impulses travelling along afferent nerves from the surface of the body generally, or from certain parts where **special sense organs** are situated. There must be—

1. Some **external stimulus** capable of affecting—
2. A **receptor.**
3. A **nerve** or **nerves** conveying impulses from this receptor to the brain.
4. A group of **nerve cells** in the brain capable of receiving and interpreting the impulses.

It must be borne in mind that the nerves which convey the impulses from the receptor to the brain do so *without any discrimination*. That is, they take no part in determining the *nature* of the sensation. Their function is to 'notify' the brain that the particular receptor from which they come has been stimulated. This message for each particular receptor is always transmitted to the same group of cells in the cerebrum, and partly by heredity, partly by training, the brain 'learns' to know where the messages come from and what they imply; and thus we become conscious of a sensation. If it were possible to cut and transpose the peripheral ends of the olfactory and the optic nerves, and the transposed nerves were able to function, then, when light fell upon the retina, we would be conscious of a smell, and when an odour permeated the olfactory mucosa we would be conscious of the sensation of light. Further, if any sensory nerve be stimulated anywhere in its course by mechanical, electrical or chemical means so as to set up a nerve impulse, then that impulse will be assumed by the brain to come from the *receptor* to which the nerve is connected, and will give rise to the sensation of light, sound, taste, etc., as the case may be.

The sensations are conveniently divided into two main groups: common sensations and the special senses.

Tactile and Common Sensations.

The so-called 'sense of touch,' mediated by nerve endings situated on the surface of the body (skin, mucous membranes, and subcutaneous tissue), is in reality composite. The common tactile sensations, usually pressure, but also including tickling and itching and the sensations of warmth and of cold, are included under common sensation. The sense of pain, which can be called forth by stimulation of the same regions, is probably in a different category, as being capable of excitation by stimulation, not only of nerve endings, but also of afferent nerve fibres in their course. The sensation associated with muscular

effort—so-called muscular sense—largely mediated by special nerve endings in muscles, tendons, and joints, is often grouped with common sensation.

Four different qualities of sensation are associated with the skin: (1) Simple contact or pressure, (2) warmth, (3) cold, and (4) pain. Careful observation shows that each of these has a punctate distribution. Only certain localised spots—pressure-spots, warmth-spots, etc.—give rise on stimulation to their particular sensations. These facts indicate that the nerve endings for each particular quality of sensation are distinct.

THE SENSE OF CONTACT is that elicited when the skin is lightly touched, as with the point of a pencil or a wisp of cotton wool. The sensation passes into one of pressure if the contact is made firmer. The existence of pressure-spots can be demonstrated by using light hairs to effect the contact. By means of these it is found that the minute sensitive areas occur as islands in the midst of insensitive parts. The spots most sensitive to touch lie close to the hairs. Sensitivity to touch may be determined in two ways. In one the minimum pressure necessary to evoke the sensation is measured. By this test the forehead and the palm are found to be highly sensitive. In the other method the skin is touched simultaneously with two points at a varying distance apart. According to the distance at which a double contact is perceived, one may grade the acuity of the sensation (**tactile discrimination**). By this test the tip of the tongue and the point of the fingers are found to possess an enormously greater discrimination than, say, the skin over the back of the neck.

SENSATIONS OF TEMPERATURE.—When the skin is touched by a body hotter or colder than itself, a sensation of heat or of cold is produced. In every case the quality of the sensation—*i.e.*, whether of heat or of cold—depends not upon the absolute temperature of the touching body, but on that of the skin at that moment. Thus, to a cold hand a cool body may appear warm provided its temperature *is* just greater than that of the hand. The same body

would appear cold to a warm hand. For this reason our sensations form a very unreliable guide as to actual temperature.

As with touch sensations, so the sensations of heat or of cold are confined to small areas scattered over the cutaneous surface of the body. The number of cold-spots is considerably greater than that of warmth-spots.

PAIN SENSATIONS.—Excessive stimulation by extremes of temperature or by great pressure may occasion the feeling of pain. At the same time there are a very large number of pain-spots situated all over the skin, which can be excited by relatively weak stimulation, as by a fine needle. In some parts of the body—*e.g.*, the pulp and dentine of the teeth, the cornea—pain is the only sensation elicited by contact. While the sense of pain is best developed in the skin, it is also associated with certain of the deeper structures. For the latter, however, the stimulus must be adequate. Mere cutting of muscle, of a vein, or of the intestine with a knife is unassociated with pain. The adequate stimulus for the pain sense of the hollow viscera is **stretching** or distension. If a piece of gut is distended with gas, the pain may be acute. In certain diseases the sense of pain may be absent over considerable areas of the skin while the sense of touch is still preserved.

Observations made after section of cutaneous nerves of the human subject have shown that the area of skin supplied by the nerve showed defects in seven distinct functions: four sensory—namely, sensibility to touch, cold, heat, pain; and three motor—namely, vaso-motor, pilo-motor, sudo-motor (sweat secretory). The sensory changes showed a central area of profound loss, an area of moderate extent surrounding this of partial loss, and a large area in which a qualitative change alone could be detected (Trotter and Davies). After section of a nerve, function may be restored, but only slowly and imperfectly. The recovery of vasomotor tone is early and is the first to return. The other functions make a gradual reappearance (see p. 27).

MUSCULAR SENSE.—By means of this we gauge especially the resistance to movements of the limbs and determine their position in space. Voluntary muscular movements are associated with the sensation of effort, graduated according to the strength of the contraction. Some authors have held that the origin of this sense is central, but the existence of a number of special end-organs in muscle, tendons, etc., leads us to believe that these sensations are peripherally excited. Abnormalities of the muscular sense may be detected by utilising a series of objects all of the same size and shape but of different weights.

SPECIAL SENSES

The special sense organs are peculiarly adapted for the purpose they have to serve. Their threshold of stimulation for the particular sensation for which they are intended is very low. By this is meant that whilst the sensation of 'light' can be evoked by the mechanical or electrical stimulation of the retina, such abnormal stimulation has to be far in excess of that necessary when light itself is allowed to fall upon the retina.

The special senses are those of smelling, tasting, hearing and seeing. The organs for these are all situated in the head, and they vary in their complexity, those for the sensations of smell and taste being the simplest in structure. All these **special sense organs** contain **modified epithelial cells,** mainly epiblastic in origin. These are in direct or indirect connection with processes of a nerve cell (so-called **bipolar cell**), from which a process passes in the opposite direction (centripetally), and arborises around processes of another cell, from which an axis cylinder passes to the central nervous system through relays.

SMELL.

THE ORGAN OF SMELL.—The **olfactory region** of the **nasal fossæ** occupies the upper part of the nose. The mucous membrane covering the upper and middle

turbinate bones as well as of the upper part of the septum is thick and pigmented (yellow), and has a **columnar** non-ciliated **epithelium**. The surface of the olfactory mucous membrane is kept moist by a large number of serous glands. Between the columnar cells there are specially modified *nerve* cells (**olfactory cells**), which terminate on the surface of the mucous membrane in bundles of hair-like processes. The columnar cells act as supporting structures for the olfactory cells. The proximal ends of the olfactory

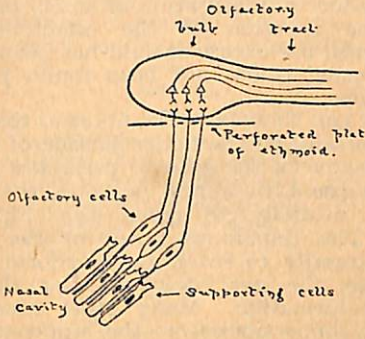


FIG. 46.—DIAGRAM OF OLFACTORY CELLS AND THEIR CONNECTIONS. (Not to scale.)

cells taper and are continuous with the nerve fibres of the olfactory nerve. These nerve fibres, which are non-medullated, pass through the cribriform plate of the ethmoid bone, and end in the **olfactory bulb** in an arborisation (**olfactory glomerulus**) with the dendrons of large '**mitral**' cells, the axons of which pass to the olfactory *tract*.

THE SENSATION OF SMELL is the result of stimulation of the terminal 'hairs' of the olfactory nerves. This is brought about by the entrance of minute particles of odorous matter into the upper part of the nasal cavity, and their direct contact with the olfactory cells; hence the sensation of smell is intensified by the

sudden indraft of air bearing odorous particles, as in sniffing.

As a single grain of musk will give out a powerful smell for years, and render the air odorous to a considerable distance, the particles are evidently very minute, and may even be gaseous. Further, they may be dissolved by the moisture on the surface of the mucous membrane, and so brought into more intimate contact with the olfactory cells. Even this is, however, uncertain, as the introduction of an odorous fluid into the upper part of the nasal cavity does not produce any sensation of smell, but entirely suspends the function of the olfactory mucous membrane until the excess of fluid has been removed.

Unlike 'taste,' it has not been found possible to classify odours.

COURSE OF THE NERVES.—The fibres of the olfactory tract pass dorsally on the under surface of the brain, and in the region of the *anterior perforated spot* some of them synapse with a new neurone, the axons of which pass medially to reach the hippocampal formation. The remaining fibres of the olfactory tract pass laterally to reach the pyriform area and there synapse, the new axons passing also to the hippocampal formation. Many other areas of the brain receive connections from the hippocampus.

TASTE.

The sense of taste is practically limited to the **taste buds,** which are found chiefly in the **circumvallate,** but also in the **fungiform papillæ** of the tongue, and scattered in the mucous membrane of the **palate** and **fauces.** The taste buds contain certain **gustatory cells** around which the terminations of the fibres of the **glossopharyngeal** and **lingual nerves** arborise. For description see p. 95.

The gustatory sensations have been classified as **acid, saline, bitter,** and **sweet** tastes. The various **flavours** are not tastes, but are *odours,* and are the result of stimulation of the **olfactory** nerve. The evidence for this is that they are not perceived when

the nose is held closed, or when the olfactory mucous membrane is deranged.

The sapid substances, which excite the terminations of the nerves of taste are dissolved in the saliva, and so act—probably by actual contact—upon the nerve terminations.

The nerves of taste to the tongue are derived from two sources: the posterior third of the organ is supplied by the ninth cranial nerve, the anterior two-thirds by the seventh. In other words, the same nerves that supply the salivary glands with secretory fibres supply the tongue with taste fibres. The fibres from the anterior two-thirds are carried at first in the lingual nerve, reaching the seventh by the chorda

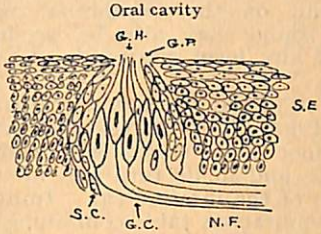


FIG. 47.—DIAGRAMMATIC SECTION OF TASTE BULB.

G.H., *G.P.*, *G.C.*, gustatory hairs, pore and cells; *S.C.*, supporting cells; *N.F.*, nerve fibres proceeding to lingual or glossopharyngea nerve; *S.E.*, stratified epithelium of tongue.

tympani. They have their cell-stations in the geniculate ganglion. The fibres of the posterior third are conveyed throughout in the glossopharyngeal. Apart from these fibres, which are connected with the taste-buds, nerves of common sensation reach the tongue from the fifth cranial nerve.

Most 'tastes' depend upon the sense of smell rather than of taste.

COURSE OF THE NERVES.—The taste fibres in the lingual and the glossopharyngeal nerves proceed to the *tractus solitarius*, and there synapse with the

second neurone, the axon of which crosses to the medial fillet of the opposite side, and ends in the optic thalamus. From there the final neurone proceeds to the hippocampal formation.

CHAPTER XVI

THE EAR AND THE SENSE OF HEARING

SOUND is a subjective phenomenon which is produced by the activity of the nervous system, and results from a mechanical impact of vibrating particles of air on the membrana tympani. The sensation of sound may also be produced by the application of any form of stimulus to the auditory nerve.

The vibration of the membrana tympani causes the ossicles (see Fig. 48) to move backwards and forwards. The foot of the stapes is in relation with the fenestra ovalis, and in its turn sets up vibrations in the perilymph of the internal ear. Immersed in this lymph is a membranous table containing the receptor mechanism which on being stimulated by the vibrations sends nerve impulses to the brain. These are interpreted as sound.

The various parts of the ear will now be considered in detail.

THE EXTERNAL EAR.—In animals in which the external ear is more largely developed than in man, it undoubtedly serves the purpose of a **collecting organ,** reflecting the sound vibrations to a focus in the auditory meatus, and so intensifying their action on the membrana tympani. In man it must be regarded as a rudimentary structure, the evidence derived from the accidental loss of this organ showing that it has no material influence in the collection of sound waves.

THE MEMBRANA TYMPANI.—Owing to the small size and varying tension of the different parts of this

membrane, it is moved by the sound vibration *as a whole*, and does not, therefore, produce a note of its own—that is, it does not vibrate in sympathy with

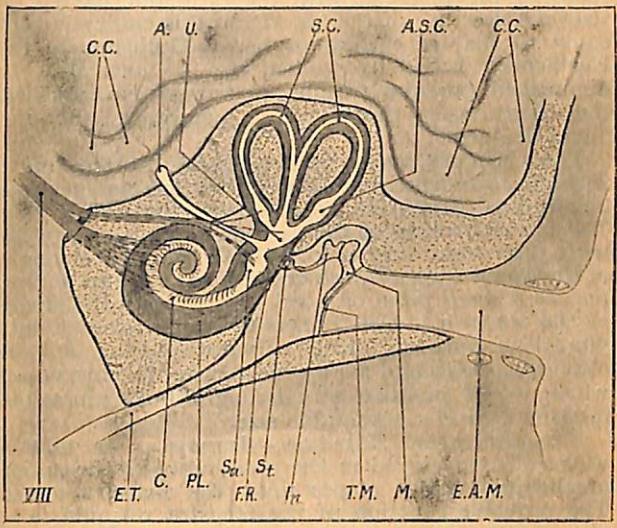


FIG. 48.—A DIAGRAMMATIC SECTION OF THE EAR, TO SHOW THE RELATION OF THE TYMPANIC MEMBRANE, THE OSSICLES, AND THE INTERNAL EAR.

T.M., Tympanic membrane; *E.A.M.*, external auditory meatus; *M.*, malleus; *In.*, incus; *St.*, stapes (in foramen ovale); *F.R.*, foramen rotundum; *E.T.*, Eustachian tube; *C.C.*, cerebral convolutions; *C.*, cochlea; *Sa.*, saccule; *U.*, utricle; *S.C.*, semicircular canals; *A.S.C.*, ampulla of semicircular canal; *A.*, enlarged end of aqueductus vestibuli; *P.L.*, perilymph; *VIII.*, the auditory or eighth nerve arising from its cochlear and vestibular roots.

vibrations of any particular period. Its tension is capable of being regulated by the action of the **tensor tympani muscle,** and its vibrations are checked by

the ossicles, so that no after-sound remains from its continued vibration after the sound waves by which it is moved cease to act upon it.

The EUSTACHIAN TUBE serves to connect the interior of the pharynx with the tympanic cavity, so that the pressure of the air within this cavity is kept equal to that of the atmosphere. Occlusion of the Eustachian tube, by giving rise to increased or diminished pressure within the tympanum, restricts the vibrations of the tympanic membrane, and produces deafness.

The OSSICLES, as has been already stated, move with the tympanic membrane; they are not set into longitudinal vibrations like the stem of a stethoscope. The physical cause of this is their thickness together with their small size in comparison with the length of the sound waves by which they are set into action: just as a *small* piece of wood is moved by the waves of the sea, whilst the timbers of a ship are set into vibrations without being actually moved, so the ossicles move to and fro by the action of sound waves which would produce actual longitudinal vibrations in structures of considerable size.

THE FENESTRA ROTUNDA.—Impulses, or minute waves, are developed in the perilymph by the action of the **foot of the stapes** upon the **fenestra ovalis.** The probable function of the fenestra rotunda is to allow of the free movement of the perilymph which extends from the fenestra ovalis, through the vestibule and cochlea, to the fenestra rotunda. The waves set up in the perilymph are undoubtedly communicated to the endolymph, and so to the hair cells in the organ of Corti.

The INTERNAL EAR, or LABYRINTH, is a complex cavity excavated in the petrous portion of the temporal bone. It consists of the **vestibule, semicircular canals** and their adnexa, and the **cochlea.** In the interior of this cavity the **membranous labyrinth** is situated. These bony cavities contain within them membranous replicas somewhat smaller in size than the cavities in which they lie. The membranous structures are attached to the bony walls at such

parts as nerves enter them, and also along the convex borders of the semicircular canals and to the lateral wall of the cochlea. Otherwise they are detached. All the cavities within the membranous structures and between them and the bony walls are filled with lymph. That inside the membranous labyrinth is called **endolymph;** that outside, **perilymph.**

The Structure of the Cochlea.

The cochlea is **a spiral canal** which has been compared to a snail-shell. It makes two and a half turns round a central column—the **modiolus.** A bony ridge, the **lamina spiralis ossea,** projects from the modiolus and partly divides this canal into two; the upper portion is called the **scala vestibuli,** and the lower the **scala tympani.**

The two scalæ are separated from each other by a membranous tube which extends from the base of the cochlea to near the apex. Here the scala vestibuli communicates with the scala tympani.

The membranous tube, from the manner of its attachments to the bony walls, acquires a triangular shape when seen in cross-section. The lower, thicker portion of this tube is called the **membrana basilaris,** and its upper and thinner part, the **membrane of Reissner** (Fig. 50).

The space enclosed in the membranous tube, known as the **scala media,** contains endolymph, and is connected with the rest of the membranous labyrinth by the **canalis reuniens,** the **saccule,** and the **aqueductus vestibuli** (see Fig. 49). It contains the **organ of Corti.**

The Organ of Corti is a complex apparatus connected with the terminations of the **cochlear branch** of the **auditory nerve.** It is situated upon the membrana basilaris. It consists of a long row of arches, formed by the **rods of Corti.** These are highly refractive elastic rod-like cells, having protoplasm only at their bases. There are about 6,000 inner rods and 4,500 outer rods, so placed that a tunnel is

left between them and the basilar membrane, the cross-section of which is more or less triangular.

Commencing at the lamina spiralis ossea and finishing at the outer part of the membrana basilaris, the following structures may be seen:

1. A layer of epithelial cells, which become heaped up, as it were, on the inner side of the inner rods of Corti; the cells which rest against these rods have stiff bundles of hair-like processes projecting from

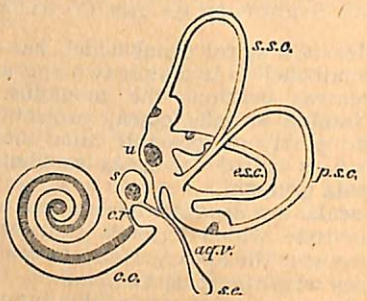


FIG. 49.—A DIAGRAM OF THE MEMBRANOUS LABYRINTH.

u, The utricle; *s*, the saccule—both contained in the cavity of bone called the vestibule; *s.s.c.*, *p.s.c.*, *e.s.c.*, the three semicircular canals; *c.c.*, the canalis cochleæ; *c.r.*, canalis reuniens, connecting the canalis cochleæ with the saccule; *a.q.v.*, the aqueductus vestibuli, uniting the saccule with the utricle. The black spots represent the portions in which the hair cells are situated.

them; they form a single line, and are the inner hair cells.

2. Next to these are the **inner rods of Corti,** which are shaped very like a human ulna, the sigmoid notches of which support the heads of the **outer rods of Corti.** The outer rod is shaped something like a swan's neck and beak; the back of the swan's head articulates with the notches in the heads of two inner rods.

3. On the outer surface of the outer rods of Corti several rows of hair cells are situated; these are

covered by a fine reticulated net, attached to the beak of the outer rod, through which the bundles of hairs project. The outer hair cells are in contact on their outer side with a layer of cubical epithelial cells, called the supporting cells of Deiters.

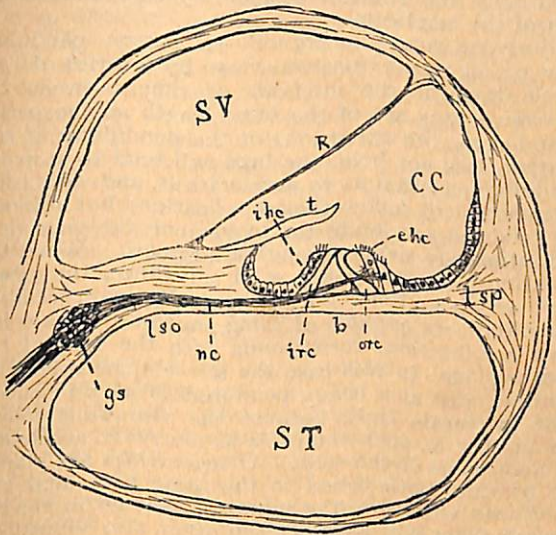


FIG. 50.—A DIAGRAMMATIC TRANSVERSE SECTION THROUGH ONE OF THE TURNS OF THE COCHLEA.

SV, Scala vestibuli; *R*, the membrane of Reissner; *CC*, canalis cochleæ; *ST*, scala tympani; *gs*, ganglion spirale; *lso*, lamina spiralis ossea; *t*, membrana tectoria; *irc*, inner rods of Corti; *orc*, outer rods of Corti; *b*, membrana basilaris; *ihc*, inner hair cells; *ehc*, external hair cells; *lsp* ligamentum spirale; *nc*, fibres of cochlear nerve.

The portion of the **auditory nerve** which supplies the cochlea lies in a canal in the axis of the modiolus, and gives off numerous branches; these run outward, through canals in the lamina spiralis ossea, and end around the inner and outer hair cells. The membrana

basilaris becomes wider in its passage upward in the cochlea, and the rods of Corti become longer.

The movements of the hair-like processes initiate impulses which travel through the fibres of the auditory nerve to the medulla oblongata, to reach eventually the **superior temporo-sphenoidal convolution** of the cerebrum.

SYMPATHETIC VIBRATIONS.—A heavy pendulum may be set into extensive swings by a series of very gentle taps, if the intervals of time between the successive taps are of the same length as the period occupied by the excursions of the pendulum; if this relation does not hold, the taps will tend to stop the pendulum as often as to accelerate it, and no visible movement will follow their application; but if every tap tends to accelerate the movement, the pendulum will ultimately swing through a large arc. When the vibrating air falls upon a solid substance, the vibrations set up in the solid are generally inappreciable, unless the note capable of being emitted by the solid, when in vibration, corresponds with the note of the vibrating air; in this case the air sets the solid into vibration, just as a heavy pendulum is set into movement by gentle taps, because the vibrations follow one another at such intervals as always to accelerate the movement of the solid. If two strings are placed side by side, both tuned to the same note, and one be set into vibration, the vibrations set up in the air between them will soon set the other into vibration; the one is said to produce sympathetic vibrations in the other.

If the student stands before an open piano and sings any note before the strings, the dampers being raised, he will find that certain strings, and only certain strings, are set into vibration, and will re-echo his voice; this is due to those strings having times of vibration which correspond to the vibrations of his voice.

These observations form the basis of **Helmholtz's resonance theory** of hearing. This states that the membrana basilaris is to be regarded as consisting of a series of strings stretched between the lamina

spiralis and the outer wall of the cochlea; for although it is not divided into separate strings, its vibrations would be similar to those of a series of strings. The rods of Corti, which rest over certain portions of the membrane, are set into vibration by sound waves corresponding to the varying width of the membrane, and so different nerve fibres are set into activity by different sounds. If this be so, the organ of Corti is an instrument for analysing or separating the mixed vibrations which fall on the ear and converting each set into corresponding nerve impulses.

Helmholtz's theory has received support from experimental investigations which have demonstrated the existence of a resonant structure within the cochlea. Other hypotheses have been put forward, but no one by itself satisfactorily explains all the phenomena associated with the interpretation of sound.

The Nature of Sound.

The nature of our consciousness is such that we are at once impressed with the idea that a **sound,** such as we hear, proceeds from the string, tuning-fork, or other instrument capable of exciting a particular form of movement in the air. There is, however, only a movement of air outside us; the sensation we call sound depends on the relation of this movement to the mechanism of the ear and the nervous system. Everything which we feel is a sensation, and as we are the subjects acted upon, all sensations are called **subjective** phenomena; the causes producing the sensation are objects which act upon us: the causes producing the sensation are therefore called **objective.**

Sensations of sound are distinguished by three characters: **loudness, pitch,** and **quality.** These are subjective characters. The movements of the air which produce the sensation of sound also possess three characters, which correspond to loudness, pitch, and quality respectively.

The Loudness or strength of a sound depends on

the *amount* of compression and expansion produced in the air around the sounding body. For instance, the wider the swing of the prongs of a tuning-fork, the more forcibly will the air in its vicinity be compressed, and the louder will be the note which is generated.

PITCH.—The *number* of vibrations which occur in a given time determines the pitch of the sound. A pendulum of a given length, when acted upon by the force of gravity alone, always takes the same time to complete its swing, whether it swings through a small arc or a large one; so a string of a given length, thickness, and tension has its own period of vibration, and produces a note, or sound, having a given pitch, whether its movements be great or small.

QUALITY OR 'TIMBRE.'—The quality of a sound depends on the manner in which the vibrations of the sounding body succeed each other. If the succession of disturbances in the air is irregular, the sensation which results is of no particular pitch; it is then spoken of as a **noise.** There is no orderly succession of movements in the membrana tympani, or in the ossicles, and the impulses set up in the auditory nerve are also irregular.

When the succession of vibrations is regular and orderly, a **musical note** is produced. When the vibrations are simple—that is, every wave rises and falls regularly and evenly—the note is said to be **simple;** a tuning fork gives a simple note. More usually the waves are complex—that is, small waves are superimposed on larger ones, just as small waves rise and fall on larger ones on the surface of the sea. The sound is then **compound;** the fundamental note is accompanied by various **overtones** or **harmonics.** The component vibrations of a musical note, such as is emitted by a vibrating string, can be heard by a practised musical ear. The number and relative strength of these give the character to the sound, and account for the **difference in quality** of the same note sounded, for example, on a flute, a violin, and a piano.

All these variations of movement are imparted to

the membrana tympani, and by it, through the ossicles, to the fluid in the labyrinth and the hair cells in which the auditory nerve terminates; and these modifications correspond to the characters of the sensation—that is, they are the external causes which give rise to the corresponding qualities of the sensation.

HARMONY AND DISCORD.—When successive or simultaneous sets of vibrations fall upon the membrana tympani, the sensations produced are productive of pleasure if the number of vibrations in each set are in simple arithmetical ratio to those of the other sets: for instance, if thirty vibrations in a second are followed or accompanied by forty, sixty, or ninety, the effect produced in the mind is harmonious; if the ratio is not simple—for instance, if sixty vibrations are followed or accompanied by sixty-two vibrations—the effect is painful and discordant. Harmony and melody depend on the simple ratio of simultaneous and consecutive vibrations.

THE MUSICAL SCALE.—From the foregoing, it follows that the only sounds which are useful in music are those depending upon vibrations the times of which bear a **simple relation** to each other. The simplest ratio is 1 to 2. When the number of vibrations is doubled, the two notes are octaves. If the relation is 2 to 3, the notes are said to be fifths.

The ear is capable of hearing vibrations as musical notes only between certain limits; a single vibration produces the sound of a tap or blow, and each vibration is heard as a separate tap or blow until 16 or more occur in every second of time; then a continuous sound results, the vibrations of which are no longer separable to the sense of hearing. The lowest note on the organ is usually produced by a pipe 16 feet long, which gives 32 vibrations in a second; this note is named $C_{,,,}$. An 8-foot pipe gives its octave with 64 vibrations, $C_{,,}$. The double octave, $C_{,}$, has 128 vibrations in a second, and so on. The highest note which is audible is said to have about 40,000 vibrations in a second, but such a note is too feeble to have any musical value.

Between a note and its octave musicians recognise 11 notes, which are separated from each other by intervals, called semitones; of these semitones, 7 only have sufficiently simple ratios to harmonise with each other; the 13 notes of a scale, including the fundamental note and its octave, are, however, needed, because the mind retains the sound of the first note struck, the keynote; and different semitones are required for different keynotes.

The following are the number of vibrations for those notes which have the simplest ratios, in the scale which has C for its keynote, in the middle compass, or that which corresponds to the middle notes of the human voice:

C with 256 vibrations in a second.
E the third to C with $\frac{5}{4}$ 256 = 320 vibrations in a second.
G the fifth to C with $\frac{3}{2}$ 256 = 384 vibrations in a second.
C′ the octave to C with $\frac{2}{1}$ 256 = 512 vibrations in a second.

The ratios of the other notes are more complex, and form less pleasing combinations.

The ear of a good musician at once detects a difference of $\frac{1}{32}$nd of a semitone—that is, one vibration in a second, more or less, would produce a different sensation in this part of the scale.

The Vestibular Apparatus.

Situated within the inner ear there is found, in addition to the cochlea, a series of structures collectively known as the **vestibular apparatus.** These consist of the semicircular canals, the utricle and the saccule. They are concerned with the equilibration of posture and locomotion.

The **semicircular canals** are three in number in each ear, and are named superior, posterior and horizontal respectively. They are so arranged that the first two are in a vertical plane and are set at right angles to each other. The third canal is placed horizontally and at right angles to the other two. These bony canals have a swelling or **ampulla** at one end, and a membranous lining which is adherent only

to part of the wall. The receptor mechanism, **crista acustica,** is situated in the ampulla. The inside of the membranous tube is filled with endolymph, and the space surrounding it with perilymph.

These canals are arranged around and in relation to a hollow structure known as the **utricle.** Adjacent to these, and in connection with them, is a smaller cavity called the **saccule** (see Fig. 49). Both the utricle and the saccule also have a membranous

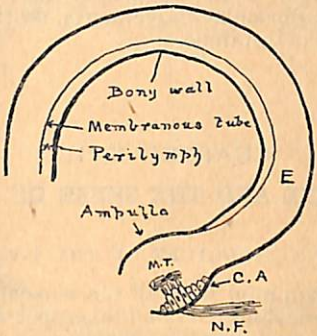


FIG. 51.—DIAGRAMMATIC SECTION OF SEMICIRCULAR CANAL.

E. endolymph within the cavity of the membranous tube; M.T., mucus tuft (cupula) resting on hair cells; C.A., crista acustica; N.F., nerve fibres of vestibular division of eighth cranial nerve.

lining, in the wall of which a receptor known as a **macula** is found.

These various receptors contain hair cells surmounted by a tuft of mucus, and any movement of the head causes a disturbance in the endolymph, which irritates the hair cells. At the base of these cells are distributed nerve fibres from the vestibular division of the eighth cranial nerve. Disturbance of the hair cells initiates nerve impulses which are transferred to the cerebellum and to the nucleus of Deiters in the hind-brain. The result of these impulses is

reflected in adjustments made in the postural muscles via the rubro-spinal and the vestibulo-spinal tracts.

When the semicircular canals of a bird are injured, it can no longer balance its head upon its neck. When the **horizontal** canals are destroyed, the head rotates from side to side; if the **vertical** canals are injured, nodding movements occur. In **Ménière's disease,** which affects these structures, the power of balancing the body is lost, the patient suffers from a sense of rotation or falling, which he endeavours to counteract by muscular movements, so that his equilibrium is not maintained.

CHAPTER XVII

THE EYE AND THE SENSE OF SIGHT

The Structure of the Eye.

The eye in common with all the sensory receptors is a structure possessing nerve endings specially modified to subserve its own purpose, in this case to detect the incidence of light waves. In order that the stimulus be particulate rather than diffuse there is interposed between the source of light and the nerve endings an optical arrangement whereby a sharp picture falls upon the sensitive area. All descriptions of the structure of the eye are merely elaborations of these fundamentals.

There are many points in common between a camera and the eyeball. In both there is an outer casing to maintain rigidity, through which the light can enter only by a special aperture. In both there is an optical system to create a picture, and in both a sensitive receiving surface.

In the study of the following description of the structure of the eye considerable help will be obtained by frequent reference to the diagram appearing on page 237.

The outer coat of the eye is represented mainly by **the sclera**, which forms a large segment of a sphere of 12 mm. radius. It consists of a dense fibrous tissue, and, although usually described as opaque, is very translucent. The **optic nerve** pierces its posterior

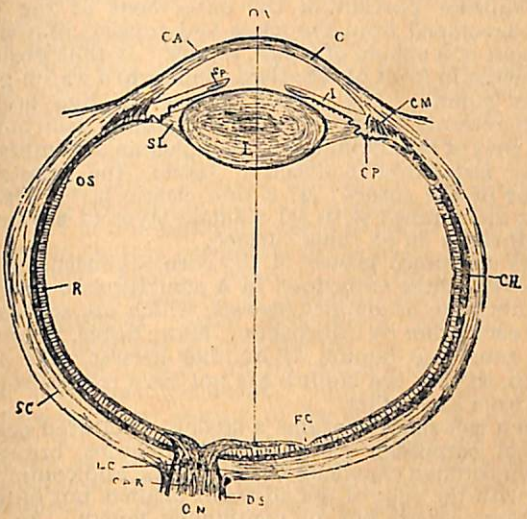


FIG. 52.—A DIAGRAMMATIC SECTION OF THE EYEBALL.

C, Cornea; *CA*, conjunctiva; *CM*, radiating ciliary muscle; *CP*, ciliary processes; *CH*, choroid; *I*, iris; *Sp.*, sphincter pupillæ; *R*, retina; *OS*, ora serrata; *FC*, fovea centralis; *CAR*, central artery of retina; *ON*, optic nerve; *DS*, dural sheath of optic nerve; *L*, lens; *OA*, optic axis; *LC*, lamina cribrosa; *SL*, suspensory ligament; *SC*, sclera or sclerotic.

part a little to the mesial side of the antero-posterior axis of the eyeball. The outer surface of the sclera is smooth and glistening, and its inner surface is covered by a thin layer of pigmented connective tissue, the lamina fusca. The anterior third of the sclera is loosely covered by a reflection of the **conjunctiva.**

which becomes firmly attached to it around the margin of the cornea, the epithelium alone, of the conjunctiva, being continued over the surface of the cornea.

The **cornea,** which is perfectly transparent, forms the anterior portion of the outer coat of the eye. It is developed from the sclera and consists of a small segment of a sphere of 8 mm. radius. It thus projects somewhat in front of the sclera, similar to a watch-glass in its mount. The cornea consists of five layers: (1) an external layer of **stratified epithelium,** continuous with that of the conjunctiva; (2) **Bowman's membrane;** (3) a laminated connective tissue, the **substance proper** of the cornea; (4) a thin elastic layer, **Descemet's membrane;** with (5) a single layer of **pavement endothelium** on its inner surface.

The substance proper of the cornea consists of interwoven fibres embedded in a structureless matrix. The fibres lie in distinct *laminæ*, which are separated from each other by cell-spaces. Many fibres, however, pass from one lamina to another between the cell-spaces, so that the laminæ are not very readily separated from each other.

Each **cell-space** contains a stellate nucleated cell, a **corneal corpuscle,** from which numerous branches extend through canaliculi in the matrix, and communicate with the cells of the adjacent lacunæ, not only in the same layer, but in contiguous layers. As the cornea is without bloodvessels, except around its margin in the immediate neighbourhood of the sclera, with which it is continuous, it is dependent on these cells for its nutrition. The lacunæ and canaliculi are not, however, entirely filled by the corneal corpuscles, but also serve as **lymph spaces,** which are permeated by nutrient plasma from the blood. The corneal corpuscles are the representatives of the connective-tissue cells of other fibrous tissues. **Nerves** from the ciliary plexus pass through the corneal tissue and are distributed as a fine plexus beneath and between the cells of the epithelium.

The Choroid Coat.—This is a very vascular membrane lining the sclerotic. It consists of a fibrous

stroma, in the meshes of which a great number of stellate **pigmented cells** are embedded. The choroid is usually described as consisting of three layers: (1) an outer layer similar to the sclera in structure; (2) a vascular layer; (3) an internal layer, in which the capillaries, pigment, and stroma are especially developed.

The Ciliary Region.—The anterior margin of the choroid is closely united to the sclera near the margin of the cornea, and a number of **non-striated muscle fibres** arise from the sclera at this point, and pass inwards and backwards into the choroid. These spread out in the choroid, so that they have a fan-like arrangement when seen in sections of the eyeball. This is the radial portion of the **ciliary muscle.** A second set of non-striated muscle fibres are arranged around the choroid peripheral to the iris and compose the circular ciliary muscle. The thick anterior margin of the choroid is plicated, and forms the **ciliary processes.** From this point forward the choroid is modified to form the iris.

The Iris is covered on its anterior surface by a single layer of epithelium, continuous with that covering the inner surface of the cornea. The space between the anterior surface of the iris and the cornea is known as the **anterior chamber,** and the annular space between the posterior surface of the iris and the lens capsule is called the **posterior chamber.** These chambers are continuous with each other and are filled with aqueous humour. The framework of the iris consists of a stroma similar to that of the choroid; the fibres are chiefly arranged radially. This stroma contains a dense **vascular network,** the principal vessels of which are radially arranged. The iris has a disc-shaped opening in its centre, the **pupil,** and it is through this that the rays of light enter the eyeball. A circular band of non-striated muscle fibres surrounds the pupil near the posterior surface of the iris—the constrictor, or **sphincter,** of the pupil. Radiating muscle fibres also exist on the posterior surface of the iris, the **dilator** of the pupil. The retinal pigment cells are continued over the posterior surface of the

iris, and form a double layer of pigmented epithelium —the **uvea.**

The Crystalline Lens is enclosed in a firm elastic **capsule.** It is biconvex, its posterior being more strongly convex than its anterior surface. The lens is formed of a series of concentric laminæ, which are denser towards its centre. These are composed of fibres, hexagonal in transverse section, which are firmly united to each other. The lens fibres are of epithelial origin. The inner face of the anterior portion of the capsule is covered by a single layer of flat epithelial cells; these become columnar around the edge of the lens, and are replaced by lens fibres behind; the transition from epithelial cells to lens fibres is gradual. The lens is divided by radial fissures into three segments; but the three fissures which divide its posterior half alternate with those dividing its anterior half. In the adult the fissures become compound; each has numerous lateral fissures, joining it at acute angles. These fissures can be seen in one's own lens by looking at a bright light through a pinhole in a piece of card, as the small beam of light entering the eye in this way throws their shadows upon the retina.

The Vitreous Humour occupies the posterior four-fifths of the interior of the eyeball. It consists of a jelly-like tissue, and is permeated by very delicate membranous septa; it is separated from the retina by a transparent membrane, the **hyaloid membrane,** which rests against and supports the inner surface of the retina.

The vitreous is in contact with the posterior layer of the lens capsule, the suspensory ligament of which is formed by the anterior margin of the hyaloid membrane.

The Retina.—The retina lies on the inner surface of the choroid, from which it obtains its nourishment. Its inner surface is in contact with a very fine membrane, the **hyaloid membrane,** which surrounds the vitreous humour.

The unit of reception in the retina is a specially modified neurone, the dendron of which is shaped like

a **cone**, or like a **rod**. The long axis of this neurone is placed perpendicularly to the surface of the retina, with the cone pointing to the back. The axon, proceeding forwards, synapses with a very short neurone,

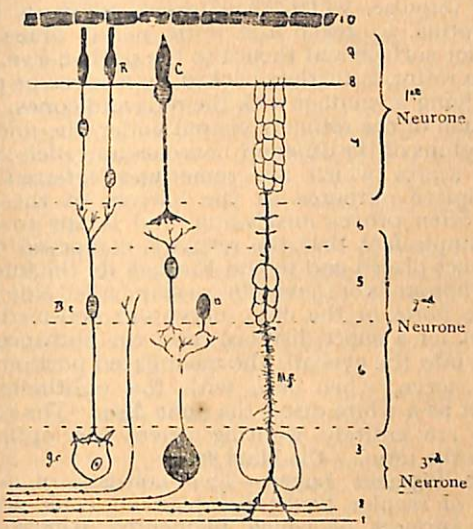


FIG. 53.—A DIAGRAMMATIC SECTION OF THE RETINA.

1, Membrana limitans interna; 2, fibres of optic nerve; 3, ganglion cell layer; 4, inner molecular layer; 5, inner nuclear layer; 6, outer molecular layer; 7, outer nuclear layer; 8, membrana limitans externa; 9, layer of rods and cones; 10, layer of pigment cells; *g.c.*, ganglion cells; *B.c.*, bipolar cells *A*, amacrine cell; *M.f.*, fibre of Müller; *C*, cone; *R*, rods.

and this in turn synapses with a third neurone the axon of which forms one of the fibres in the optic nerve.

The retina may be looked upon as being a collection of thousands of such chains of three neurones packed closely side by side, and bound together with special

neuroglia cells called **Müllerian fibres.** The really unique feature about the retina is that the light has to traverse its whole thickness before it reaches the sensitive nerve endings (rods and cones), which are situated on its choroidal surface. This initiates a nerve impulse, which then travels forwards through the retina to reach the optic nerve fibres on its anterior surface and thence to the optic nerve.

The retina is further backed by a layer of pigment cells, lying in contact with the rods and cones. When a section of the retina is viewed under the microscope the cytons of the different neurones and their synapses form strata which are sometimes referred to for descriptive purposes as the 'layers of the retina.' This often proves misleading, and is apt to obscure the simple fact that the retina is composed of three neurones placed end to end through its thickness, and that thousands of these sets are marshalled side by side.

The fibres of the optic nerve are non-medullated, except for a short distance from the entrance of the nerve into the eyeball; the medullated portions of the optic nerve, when seen with the ophthalmoscope, appear as a white disc—the **optic disc.** The rods and cones are entirely wanting where the optic nerve leaves the retina—the **blind spot.**

The Pigment Layer.—This consists of a single layer of regular hexagonal pigment cells, from the inner surfaces of which pigmented fringes extend between the outer segments of the rods and cones. The pigment is called **visual purple** or **rhodopsin.**

The Fovea Centralis and Yellow Spot.—In the centre of the retina the rod and cone layer consists entirely of cones, and the layers between it and the vitreous are very thin, giving rise to a slight pit; this is the **fovea centralis.** Around the fovea the other layers of the retina are thicker than elsewhere, and have a yellow colour—the **macula lutea.** The fovea and macula are the most sensitive portions of the retina.

The Ora Serrata and Pars Ciliaris.—Near the anterior part of the retina, the ora serrata, the various layers gradually thin out and disappear, and in front, the pars ciliaris, nothing is left but a single layer of

columnar epithelial cells. These are the morphological representatives of the whole retina in this region.

Functions of the Eye.

We become conscious of the sensation of light when certain vibratory disturbances fall upon the rods and cones in the retina. These waves of vibrations proceed in straight lines from every luminous body and they radiate outwards in a divergent manner. If, however, the source of illumination is at a distance of twenty feet or more, then those rays of light which enter the eye may, for all practical purposes, be considered parallel.

It is a fundamental condition for clear vision that the image of the object looked at be sharply delineated on the retina. In order to effect this the light rays have to be refracted or 'bent' in such a manner that they meet on the retina. This is accomplished by the optical system present in the eye, but before discussing it in detail, it will be found helpful to review the optical properties of a simple lens.

When parallel rays of light fall upon a convex lens, these rays are brought to a focus at a fixed distance behind it, known as the **focal point** (A, Fig. 54). The power of the lens to do this is determined by two factors, its *density* and its *convexity*. The greater these are, the greater the power of the lens. If, however, the incident light rays are divergent, then as the power of the lens remains constant, it will be unable to refract the rays sufficiently to bring them to the focal point. They will meet some distance behind this, as in B, Fig. 54. If, however, a *more convex* lens be used, then the divergent light rays could be brought to a focus at the same distance behind the lens as in the first instance. This is shown in C, Fig. 54.

In the eyeball the refractive system is more involved than the simple lens referred to above. Whenever light passes from one transparent medium to another of different density, the light is always deflected from

its course—**refracted,** unless the light be passing along the optical axis. The greater the difference in the density of the media traversed, the greater the refraction. Thus it comes about that when a ray of light falls upon the **cornea** it is refracted on the outer and inner surfaces, and again at the anterior and posterior

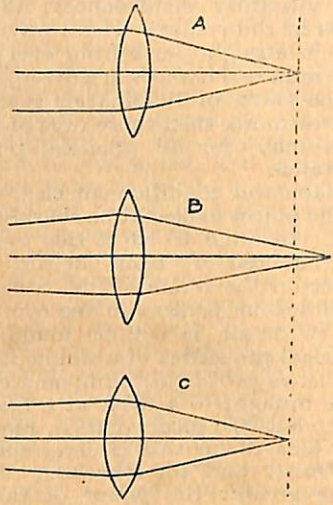


FIG. 54.—*A* AND *B* SHOW THE FOCUSSING OF PARALLEL AND DIVERGENT RAYS RESPECTIVELY WHEN FALLING UPON LENSES OF THE SAME STRENGTH. *C* SHOWS THE FOCUSSING OF THE SAME DIVERGENT RAYS WHEN FALLING UPON A MORE POWERFUL LENS.

surfaces of the lens. Although the **lens** possesses great density, its power for refraction is greatly lessened, due to the fact that on its anterior surface it is in contact with the aqueous humour, and its posterior surface abuts on the vitreous. The cornea, therefore, or more correctly the **aqueous humour,** in virtue of the curvature imparted to it by the

cornea, possesses the greatest refractive power in the above system.

The lens is supported between the two layers of the lens capsule, the periphery of which is attached by the suspensory ligament to the ciliary body. Under normal conditions when the eye is at rest the capsule is *tightly stretched* by its attachment, and as a result the lens is slightly flattened on its anterior

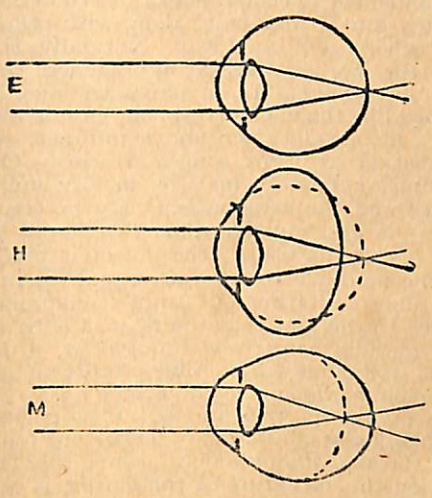


FIG. 55.—DIAGRAMS OF EMMETROPIC AND AMETROPIC EYES SHOWING COURSE OF PARALLEL RAYS.

E, Emmetropic eye; *H*, hypermetropic eye; *M*, myopic eye.

surface. Under these conditions, which obtain in the normal or **emmetropic** eye, when parallel rays of light fall upon the cornea, they are brought to a focus on the retina. It is generally accepted that the refractive power, or focal length, of the optical system in the eye varies comparatively little as between different individuals. In many people, however, the eyeball is too short in its antero-posterior

diameter, and parallel rays of light are focussed behind the retina. This condition is known as **hypermetropia,** or long sight (H, Fig. 55). Sometimes the eyeball is too long, and thus the image is brought to a focus in front of the retina. This is known as **myopia,** or short sight (M, Fig. 55). The former defect is remedied by wearing convex glasses, myopia is corrected by the wearing of concave glasses.

Astigmatism is a peculiar defect of vision of frequent occurrence, and it may exist along with other defects or in an otherwise normal eye. Normally, the curvature of the cornea closely approaches that of a segment of a sphere. In an astigmatic eye, however, it is shaped like the back of a spoon, having a maximal curvature in one direction and a minimal curvature in a direction at right angles to this. Obviously the maximal curvature may be in any meridian of the cornea and the astigmatism may be complicated by hyperopia and myopia; thus there may be many varieties of astigmatism. The defect is made manifest by the inability to see with equal distinctness a series of lines radiating out from a common point. This is due to the fact that the rays of light from the different meridia cannot be brought to a focus on the retina *simultaneously*. This results in an astigmatic person confusing such letters as a, e and c, and such figures as 3, 6 and 9. It is corrected by interposing glasses consisting of a slice cut longitudinally from the side of a cylinder. Thus, if in the vertical direction the curvature of the cornea is too small, the slice of the cylinder is placed with its plain surface transversely across the eye, so as to help out the deficient curvature of the cornea in the vertical meridian.

Accommodation.—So far we have considered the case of parallel rays falling upon the eye. This condition obtains when looking at objects twenty feet or more removed. When, however, the eye is used to look at objects nearer at hand—for example, in the process of reading—the rays falling upon the eye are now divergent. Under such circumstances, instead of a point of a near object being represented

by a point on the retina, it is represented by a small circle of light: and as the circles formed by the light from adjacent points in the object overlap, a **blurred image** is the result. In order that they may be focussed upon the retina it is necessary to *increase* the power of the lens. This is done by the process of accommodation.

Accommodation or focussing is brought about by contracting the radial and circular fibres of the ciliary muscle. This has the effect of diminishing the circumference of the ciliary body, thus lessening the tension on the lens capsule. The lens, in virtue of its inherent resilience, now becomes more convex by the bulging forward of its anterior surface. It thus becomes more refractive, in a degree sufficient to bring the rays of light to a focus on the retina. This, the generally accepted theory, is that propounded by **Helmholtz,** and it should be noted that the lens is allowed *passively* to alter its shape by the diminution in the tension of the capsule. **Tscherning**, however, has suggested that accommodation is produced by *increased* tension on the lens capsule. This causes a flattening of the *periphery* of the lens, and as the central portion is more resistant, the curvature of the anterior surface is thereby increased. The **nerves of accommodation** are those supplying the ciliary muscles. They belong to the **parasympathetic** system, and leave the midbrain in the third cranial nerve. Their cell station is in the ciliary ganglion, whence they emerge in the **short ciliary nerves** to reach the eyeball. From the foregoing, it will be apparent that the nearer the object, the greater will be the requisite contraction of the ciliary muscle and consequent bulging of the lens, to produce a distinct picture on the retina.

The *shortest* distance for which the eye can be accommodated is called its **near-point.** In children the near-point of the normal eye is about 3 inches from the cornea; it is gradually removed with age, so that at fifty it is usually 16 inches, and at sixty 40 inches, from the eye. This is due to the gradual loss of elasticity in the lens and the structures around

it. Loss of power of accommodation is called **presbyopia.** In very old people all power of accommodation is usually lost. The presbyopia is then said to be absolute. Convex spectacles are used to supplement the power of accommodation in presbyopia, and enable near objects to be seen distinctly.

The Visual Axis.—A line projected from the fovea centralis of the retina, and passing through the optical centre of the eye, is called the visual axis. It does not coincide with the optical axis, which commences from a point on the retina more mesially placed.

Convergence.—The visual axes of the two eyes are always directed towards the point to which we are looking; hence they are practically parallel in looking at distant objects, but converge when we look at near objects, owing to the rotation of both eyes inwards by the action of the internal recti. Should this convergence not be correct then **diplopia** or double vision results, a condition found in squint.

The Functions of the Iris.—The iris has three distinct functions: (1) It prevents spherical aberration; (2) it assists in producing a sharp image during accommodation; and (3) it regulates the amount of light which falls upon the retina.

Spherical Aberration.—The focus of the rays of light which fall upon the edges of a spherical lens is shorter than that of those which fall upon its central portion; hence opticians always place a perforated diaphragm in front of a lens to cut off the peripheral rays, which would otherwise tend to confuse the image produced. This defect of lenses is spoken of as *spherical aberration.* The refractive media of the eye are not free from this defect; and the **iris** serves the purpose of a **diaphragm** in an optical instrument, and prevents the blurring of the images on the retina, which would otherwise arise from spherical aberration. Spherical aberration is greater with pencils of diverging than with pencils of parallel rays.

The iris increases the sharpness of the image during accommodation. The **sphincter muscle** of the **pupil contracts in association with the ciliary muscle,** so that the diameter of the pupil is diminished in

looking at near objects. If the pencils of light came to an actual point upon the surface of the retina, the focus of a large cone of light would be as accurate as that of a small cone; but during accommodation the actual focal point must be regarded as a 'circle of diffusion' near the apex of the pencil. **Contraction of the pupil during accommodation** diminishes the size of the circles of diffusion, so that the vision is rendered clear with a less exact accommodation than would be needed with a dilated pupil, whilst it also corrects the increased aberration arising from the divergence of the rays of light from near objects.

The iris regulates the amount of light which falls upon the retina. The **sphincter muscle contracts reflexly** when a strong light falls upon the retina. This reflex is bilateral, owing to some of the fibres of the optic nerves decussating in the optic chiasma, and so if light strikes one eye, the pupils of both eyes will contract. Afferent impulses travel to the corpora quadrigemina through the optic nerve, and produce efferent impulses which stimulate the parasympathetic fibres emerging in the third nerve with resultant contraction of the pupil. Dilation of the pupil is due to impulses which originate in the ciliospinal centre, in the upper part of the spinal cord; these are probably continuous, producing tonic contraction of the radial fibres of the iris.

In addition to the foregoing the pupil is **constricted** (1) during sleep, and (2) from the action of drugs, morphia, pilocarpine. The pupil is **dilated** (1) with the removal of the light stimulus, (2) during fright, and (3) from the action of atropine.

The **nerve supply** to the **sphincter pupillæ** and the **ciliary muscles** belongs to the *parasympathetic* system. The preganglionic fibres are contained in the third cranial nerve. These end in the ciliary ganglion, and the postganglionic fibres emerge in the short ciliaries. The **dilator pupillæ** is supplied by *sympathetic* fibres which are derived from the cervical sympathetic nerve. They join the fifth cranial nerve and pass into the long ciliaries. They also constrict the bloodvessels of the iris.

Vision.

Earlier in this chapter it was stated that the sensitive layer of the retina was that containing the rods and cones. An image falling upon any part of the retina where these are absent cannot be perceived by the brain.

All the optic nerve fibres on their way to the brain pass over the surface of the retina to converge on one area where they pierce the retina and emerge from the eyeball as the **optic nerve.** This area is devoid of rods and cones, and is called the **blind spot.** It is situated about 3 mm. to the mesial side of the optical axis, and any image falling upon it cannot be seen.

To demonstrate the blind spot hold up your two thumbs, side by side, about 12 inches in front of the eyes. Close the right eye and gaze intently at the nail of the right thumb. Whilst continuing to do so, move the left hand to the side, and at a certain distance away you will be unable to see the left thumb nail. This is because its image is falling upon the blind spot in the left eye. Move the left hand up or down, inwards or outwards, and the image of the nail will reappear. The phenomenon may be conveniently demonstrated also with the letters L and R appearing below. Close the right eye and fix the gaze upon the

L R

letter R. Now move this book nearer to and further from the eyes and at a certain distance removed (about 9 inches) the letter L will disappear.

The blind spots in the two eyes are not directed simultaneously towards the same object, thus we do not lose sight of an object on account of its image falling upon a blind spot. Neither does the blind spot appear as a dark space even when looking with

only one eye, because there is no centre in the brain to be conscious of it.

Purkinje's Figures.—If a cone of light from a convex lens be thrown upon the sclerotic, near the margin of the cornea, it is possible to produce shadows of the branches of the arteria centralis retinæ upon the rods and cones. If this be done in a dark room, whilst the subject of the experiment looks at a white screen, he will see an image of the vessels of his own retina projected on the screen: the vessels seen in this way are known as Purkinje's figures. It is possible to show by measurements that the figures are actually produced by shadows on the layer of rods and cones.

Retinal Purple.—The outer segments of the rods are of a purple colour in the eyes of animals which have been kept in the dark. This colour is rapidly destroyed by the action of light, and is renewed by the retinal pigment. It may be dissolved out of the rods, and isolated. This substance is known as retinal purple, or **rhodopsin.** There is evidence, therefore, that chemical changes occur in the rods under the action of light. There is no retinal purple, however, in the cones, so that it is evidently not essential to vision. Other changes must occur, and the nerve impulses are due to these changes as well as to the bleaching of retinal purple.

Binocular Vision.—Although we have two eyes, we see but a single field of vision. There are two pictures, one on each retina, but these are mentally fused together, and a single picture is the result. **Double vision,** however, is produced as soon as the normal co-ordinated movements of the eyeballs are interfered with, as in squinting. It is a condition of single vision that the image of each object falls upon identical points on the two retinæ. The points on one retina have corresponding points on the other. Thus, the points on which the visual axes would fall give identical impressions to the mind. A point at a given distance above or below this corresponds, or is identical with, a similarly situated point in the other eye. Every point lateral to the centre of the retina of the

right eye corresponds with a point at a similar distance mesial to the centre of the retina of the left eye, and *vice versa*. Images falling on such points give rise to a single sensation; such points are named **identical points** for this reason.

Although the *points* are identical, the *images* falling upon them are not exactly similar to each other. The difference is due to the different viewpoint of each eye, some portion of an object being seen by each eye that is not visible to the other. The fusion of these two images gives the appearance of solidity and perspective, and is known as **stereoscopic vision.** By training and experience we are able to appreciate that distant objects are solid, and to estimate their probable distance from us. By utilising one eye alone our ability to judge distances is greatly handicapped. This is particularly manifest for distances a few feet removed from the eye.

Colour Vision.

Several theories have been advanced to explain the phenomena associated with colour perception, but no single theory alone can explain them satisfactorily.

The **Young-Helmholtz** theory has obtained the widest acceptance. It is based upon the assumption that there are three different photo-chemical substances contained respectively in three sets of cones in the retina, each set being responsive to a particular range of wavelength of light. One set of cones is stimulated by the very short wavelengths in the blue-violet region of the spectrum. Another set is sensitive to the longest wavelengths at the red end; and the third set is stimulated by the medium wavelengths in the yellow-green region. All three types of cones are represented in the *fovea*, but as its periphery is reached the cones responsive to yellow-green cease; next, more peripherally, the cones sensitive to red disappear; and lastly, a little further removed, the cones affected by blue colours are absent. When all the cones in the foveal region are equally stimulated

we are conscious of the sensation of white light. All other colour sensations result from the effect of the combined wavelengths acting upon the different cones in varying proportions. If the image of an object falls upon the retina outside the areas mentioned above we are conscious only of varying shades of grey.

Edridge-Green has suggested that there is no differentiation between the cones, but that each individually sends a nerve impulse to the brain, the nature of this impulse being determined by the particular wavelength of the light which falls upon the cone. This hypothesis is, however, untenable, as it postulates qualitative variations in the nature of the messages transmitted by the same nerve. This is contrary to Müller's law.

Colour Blindness is that condition where a person's range of colour perception is limited, with a co-existent inability to identify certain fundamental colours or to match standard colours presented to him. The condition, which is due to some defect in the function of the cones, is more common in males, about 4 per cent. being so affected. There are varying degrees of colour blindness, from the rare condition of total inability to distinguish any colours (everything appearing as different shades of grey), to the confusion of reds and greens. The condition may be tested for by using the Edridge-Green lamp, the test plates of Ishihara or Holmgren's wools.

Night Vision.—As has been stated, the *cones* are present in the retina in greatest concentration in the region of the fovea. No rods are found in that part. In dim light, as for example in a darkened room or out of doors in the twilight, vision at the fovea is very poor and may be absent. Objects, however, the images of which fall on the retina peripheral to the fovea, may be discerned. This is due to the fact that the rods are more easily stimulated than the cones. In the rods there is a pigment, **visual purple,** which is bleached when light falls upon it, and it is believed that this chemical change gives rise to electrical charges which initiate nerve impulses in the optic nerve. The longer light is kept from falling upon

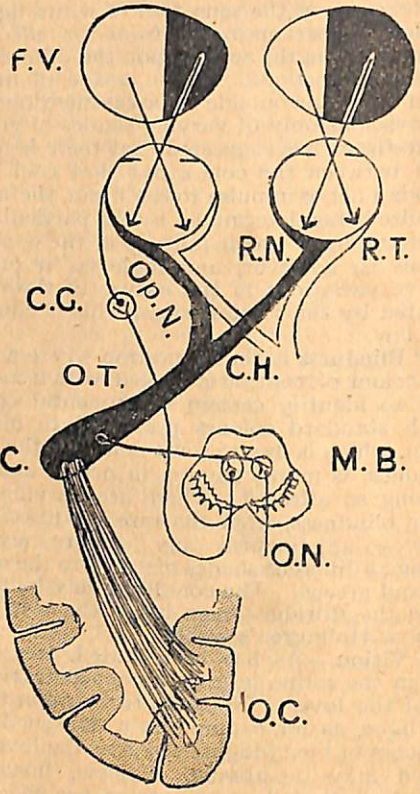


FIG. 56.—DIAGRAMMATIC REPRESENTATION OF THE PATH OF THE VISUAL IMPRESSIONS.

F.V., Field of vision; *R.N.*, nasal part of retina; *R.T.*, temporal part; *C.H.*, chiasma; *C.*, external geniculate body, anterior corpus quadrigeminum and pulvinar; *O.C.*, occipital cortex; *M.B.*, mid-brain; *O.N.*, oculo-motor nerve; *C.G.*, ciliary ganglion; *Op.N.*, optic nerve; *O.T.*, optic tract.

the retina, the greater is the accumulation of visual purple, and the eye is said to be **dark adapted.** The maximum sensitiveness is reached in about one hour. If there is an inability to manufacture this visual purple, then the subject will suffer from **night blindness,** and will be unable to find his way about in the twilight. It has been shown that a deficiency of vitamin A in the diet will produce this condition.

Nerve Tracts in Relation to Vision.

As has been already stated, the retina may be considered as being made up of three relays of nerve elements. The **rods and cones** end in processes which synapse with processes from intermediate neurones, processes from the opposite sides of these cells arborising around the processes springing from the large nerve-cells of the **ganglion cell layer.** The axons of these form the **optic nerve.** The two optic nerves meet at the **optic chiasma,** where a partial decussation of the nerve fibres takes place. The fibres from the inner or *nasal* side of each retina cross to the opposite side, and in conjunction with the fibres (uncrossed) from the *temporal* side of the opposite retina they form the **optic tract.** In this structure they are conveyed to the anterior corpora quadrigemina, and to the external geniculate body, in each case synapsing with nerve cells in these bodies. The nerve cells in the anterior corpora quadrigemina send their axons to the nuclei of both the third nerves, where they synapse with parasympathetic fibres emerging in the latter. These in turn innervate the sphincter pupillæ; by this route the **light reflex** is mediated. By this arrangement it will be noted that when light falls upon one eye only, the pupils of *both* eyes are constricted. This information is sometimes made use of when testing a malingerer who may claim to be totally blind in one eye.

The nerve cells of the external geniculate bodies send their axons, which constitute the **optic radiation,** to the occipital cortex. There the axons terminate

in regions disposed above and below the calcarine fissure. It is here that the sensation of sight is situated, the part being known as the visio-perceptive area. The brain is, however, unable to interpret or recognise the picture received without reference to another centre, the visio-psychic area, which is situated on the lateral surface of the occipital lobe (see Fig. 57). In this part is situated the memory of

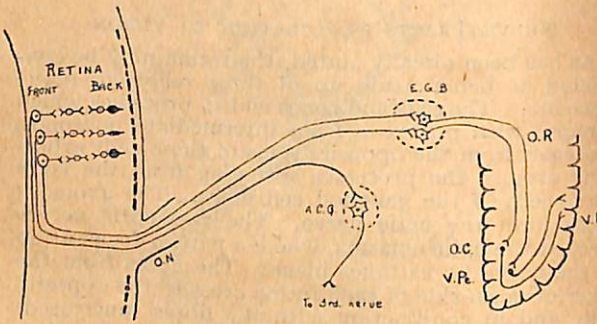


FIG. 57.—DIAGRAM TO SHOW NERVE CONNECTIONS BETWEEN THE RETINA AND THE OCCIPITAL CORTEX.

O.N., Optic nerve; *A.C.Q.*, anterior corpora quadrigemina; *E.G.B.*, external geniculate body; *O.R.*, optic radiation; *O.C.*, occipital cortex; *V.Pe.*, visio-perceptive area; *V.Ps.*, visio-psychic area.

things previously seen, and the nature of an object such as a knife, coin or key is identified as such.

From the foregoing it will be seen that the left half of each retina is represented in the left occipital cortex, the right half in the right occipital cortex. Destruction, therefore, of say the left occipital cortex, or of the left optic radiation, or of the left optic tract, will result in total blindness in the left half of *both* eyes, corresponding to the *right half of both fields of vision.* This may be more readily understood by reference to Fig. 56.

CHAPTER XVIII

THE ENDOCRINE ORGANS

SCATTERED throughout the body are glands, or groups of cells, whose secretions are destined for use in any part of the organism where they may be required. These secretions do not leave the glands by means of ducts, but pass directly into the blood stream or the lymph, and are carried throughout the body. Because of this fact, these glands were earlier referred to as the **ductless glands.** It was discovered, however, that certain glands which possessed ducts (*e.g.*, the pancreas) also contained groups of cells which secreted directly into the blood, and to meet the situation all such internally secreting glands and cells are collectively known as the **endocrine organs.** Their secretions, or according to some authorities their *incretions*, are called **autacoid substances,** commonly referred to as **hormones.** This name, however, implies a stimulating action, and as some of the autacoids are inhibitory in their effect, it has been suggested that these latter be called **chalones.**

The autacoids are of small molecular structure and are therefore readily diffusible; most of them withstand boiling, thus differing from the enzymes. The pharmacological action of these glands may be demonstrated by the injection, either intravenously or subcutaneously, of extracts of the glands or of solutions of their active principles. In a limited number of instances the action of the autacoid may also be obtained by its oral administration, but in general this is ineffective owing to the destruction of the autacoid by the digestive secretions. The physiological action of the glands when *in situ* in the body is a little more difficult to evaluate, for it is probably correct to state that every endocrine organ affects in some manner the activities of other endocrine organs. The changes, therefore, which follow the stimulation of an organ of internal secretion, or its experimental removal may not be due directly to the effect of the gland

per se upon the organism, but indirectly through its influence upon one or more of the glands which have been left undisturbed.

Thyroid.

The thyroid gland consists of two almond-shaped lobes joined by an isthmus, the whole resembling the shape of the letter H. It is situated in front of the trachea just below the level of the thyroid cartilage. Each lobe consists of numerous lobules divided into an enormous number of vesicles which are lined by

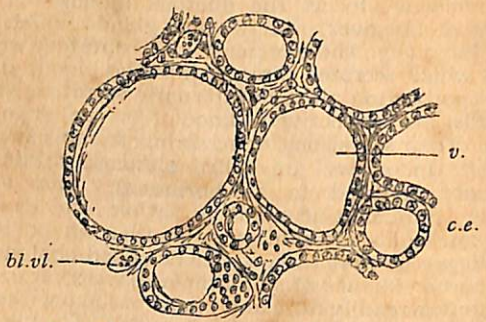
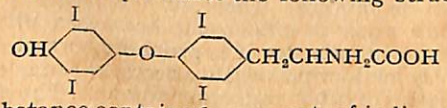


FIG. 58.—SECTION OF THYROID VESICLES.
v., Vesicle; *c.e.*, cubical epithelium; *bl.vl.*, bloodvessel.

a single layer of cubical epithelium. These vesicles contain a colloid material, **thyroglobulin,** which is rich in organically combined iodine. From this colloid there has been isolated an active principle, **thyroxine,** which possesses the following structure:



This substance contains 65 per cent. of iodine, and has now been prepared synthetically. Its relationship to *tyrosine* is seen from the following structural formula:

tyrosine

It has been calculated that the body uses up about 1 mg. of thyroxine daily. The administration of thyroxine to a subject who has had his thyroid removed will maintain his metabolic activity. There is reason to believe that thyroxine is not the only active principle in the thyroid.

It is the function of the thyroid gland to regulate body metabolism. Failure to do so during infancy will produce the condition known as cretinism; should deficiency occur in adult life, the resulting condition is called myxœdema.

Cretinism begins to show itself when the child is about six months old. The normal signs of progress are delayed. The ability to sit, walk and speak is slow in developing, and mental retardation is such that the child may become an idiot. The skeleton is stunted, and fat is deposited in excess in the upper parts of the body. A cretin at fourteen years of age may have the mentality of a child of three.

Myxœdema is the result of thyroid deficiency developing in adult life. The basal metabolic rate is much reduced; all the functions are below par. The subject feels the cold intensely, muscular movements become sluggish, and there is loss of memory and slowness of speech and thought. The skin becomes coarse and dry, the hair falls out and myxomatous deposits gather under the skin.

Cretinism may be prevented, and myxœdema may be cured, by the timely and continuous administration of thyroid gland substance, which is effective when given by mouth.

An enlargement of the thyroid gland is known as a **goitre.** There are two main types which may be conveniently designated, simple and exophthalmic. In a **simple goitre** there is usually plenty of colloid material, but it is **deficient in iodine.** The gland may reach an enormous size, and so create physical discomfort. The condition is commonly due to a deficiency of iodine in the diet, and in districts where this type of goitre is endemic it may be prevented by

the administration of small doses of iodine. As little as 0·6 g. of iodine per year is usually effective.

In **exophthalmic goitre** there is increased activity of the gland, probably accompanied by an excessive production and liberation of thyroxine. There is a large increase in the metabolic rate; increased oxidations cause increased appetite. The skin is flushed and moist, and the subject does not feel the cold readily. There is a decreased sugar tolerance, and actual glycosuria may be found in some cases. Protrusion of the eyes and retraction of the upper eyelids (**exophthalmos**) are common features. There is increased activity of the adrenals and the sympathetic nervous system, as shown by a fast pulse rate (*tachycardia*), with sometimes cardiac palpitation or irregularity and a raised blood pressure.

The functioning of the thyroid is regulated by the sympathetic nerves, and by the **thyrotropic hormone** from the anterior lobe of the pituitary. Its activity also varies in accordance with the temperature of the atmosphere, cold weather having a stimulating effect, while surrounding warmth tends to lessen its action.

Parathyroids.

The parathyroid glands are composed of epithelial cells arranged in columns. They are usually four in number, one at each pole of the thyroid lobes. Their function is to **control the concentration of the Ca and P** ions in the blood.

The active principle of these glands has not yet been isolated in a pure condition, but a potent extract (**parathormone**) has been prepared by means of extraction by acid. If suitable doses of this preparation are injected there results (*a*) an increase in the ionic calcium in the blood, (*b*) a decrease in the ionic blood phosphorus, and (*c*) an increased excretion of Ca and P in the urine. If an animal should have its parathyroid glands removed, administration of parathormone by injection will be effective in maintaining health, and will prevent the sequelæ which

follow parathyroid deprivation. Administration of desiccated parathyroid glands by mouth is ineffective.

The function of the parathyroids has been studied by the experimental removal of the glands from animals, and by their accidental removal from, or hypertrophy in, human beings. Removal of the glands produces a fall in the Ca content of the blood (**hypocalcæmia**), along with a rise in the blood phosphorus. There follows increased irritability in the peripheral motor nerves, giving rise to tremors followed by clonic and tetanic spasms (**tetany**), and death may ensue.

In **overactivity** of the glands there occurs a large withdrawal of Ca from the bones, and this element appears in excess in the blood; the surplus Ca is excreted in the urine and is lost to the body. As a result of the mineral depletion, the bones become deformed and cavitied, the condition being known as *osteitis fibrosa*.

As has already been noted, the **injection of parathormone** into normal animals will give rise to an increase in the blood Ca, and if the injections are repeated sufficiently often, a severe **hypercalcæmia** will occur, with diarrhœa, lethargy and muscular weakness, eventually culminating in death.

The Suprarenal Glands.

There are two suprarenal glands, or adrenals, one being situated in the region of the upper pole of each kidney. They are composed of a mass of epithelial cells surrounded by a capsule and subdivided by connective tissue. Each gland consists of two parts: a cortex and a medulla.

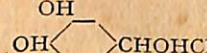
The **cortical** portion of the glands is developed from the mesoblast. In this the epithelial cells are arranged in different *zones*, named from without inwards, zona glomerulosa, zona fasciculata and zona reticulata. The **medullary** part arises from the sympathetic nervous system, derived from the epiblast. In this the cells are arranged in an irregular manner round the intercommunicating blood sinuses and sinusoids with which it is richly supplied.

The cells in the medullary portion vary in shape, and contain granules which stain a deep brown with chromates. Because of this reaction these cells are

FIG. 59.—CORTEX OF DOG'S SUPRARENAL.
c., Capsule; *z.g.*, zona glomerulosa; *z.f.*, zona fasciculata; *z.r.* zona reticularis.

referred to as **chromaphil tissue,** the staining being due to the presence of adrenaline, the active principle of the medulla.

Adrenaline is a derivative of tyrosine, and possesses the following structure:



Pharmacologically it is of great importance, but evidence has been produced which suggests that it is not essential to life. The physiological properties of adrenaline may be demonstrated by its injection into an animal. The effect produced is *similar* to that which would follow stimulation of the entire sympathetic nervous system. The more important phenomena are as follows. The coronary vessels and probably the vessels in muscles are dilated, thus causing a redistribution of the blood to the tissues utilised in exercise. The arterioles of the splanchnic and skin areas are constricted, producing a rise in the blood pressure. The pupils of the eyes are dilated and there is retraction of the upper eyelids. There is inhibition of intestinal movement and closure of the sphincters. The bronchioles are relaxed. In addition, there is an increased hydrolysis of the glycogen stored in the body, and a mobilisation of glucose in the blood. The **non-production of sweat** forms an exception to the general effect, but, as already stated on page 216, the sympathetic nerves to the sweat glands are *cholinergic*. These effects following upon the injection of adrenaline are of very short duration as the drug is rapidly oxidised in the body.

There is no evidence that in the normal individual adrenaline is being secreted under conditions of rest. This substance, however, might be looked upon as the hormone of emergency, and it has been aptly termed the drug of fright, fight and flight. It is not surprising, therefore, to learn that there are many ways, direct and indirect, by which the adrenals may be activated.

The adrenal glands are supplied by secretory fibres from the **splanchnic nerves.** These fibres have their origin in the brain stem, and are controlled reflexly. A fall in the blood pressure initiates impulses in the aorta and the carotid sinuses, which pass to the brain stem and stimulate the secretory fibres to the adrenals. An increased secretion of adrenaline follows, and the blood pressure rises. Conversely, a rise in blood pressure causes messages to be sent to the brain stem, inhibiting the activity of the secretory fibres,

the adrenaline output ceases and the blood pressure returns to a normal level.

Emotion or fright will also produce an increased output of adrenaline, and experimental observation has shown that this increased secretion is dependent upon the nerves to the adrenals being intact. It has already been noted that adrenaline stimulates metabolic changes in the body, thus increasing the heat production. It is only natural, therefore, that **exposure to cold** liberates adrenaline and so stimulates oxidation. Summarising, it may be stated that it is the function of the suprarenal medulla to maintain the blood pressure at an even level, to regulate the *distribution* of the blood, to see that the glucose content is sufficient, and to stimulate metabolism in emergencies.

The **adrenal cortex** is essential to life. Death occurs within 4 or 5 days of the removal of both adrenal cortices. The cortex is intimately concerned in the control of the ionic distribution and in particular with that of sodium and potassium. There is also evidence to suggest that the cortex enables the body to resist stress and that it is a detoxifying centre for bacterial and other toxins. In adrenal cortical insufficiency the serum sodium falls and the blood potassium tends to rise. At the same time the blood sugar is often at a lower level than normal. Degeneration of the cortices in human beings gives rise to **Addison's disease,** in which, in addition to the blood ionic changes mentioned above, there is a fall of the body temperature and of the blood pressure, wasting of muscle, extreme lethargy, gastro-intestinal upset and pigmentation of the skin. Such a person is extremely susceptible to any infection.

An active extract called **cortin** has been prepared from the adrenal cortex. This can modify the above changes, and if given in sufficient dosage can maintain life in Addison's disease and in adrenalectomised animals. Recently several crystalline substances allied to sterols have been isolated from adrenal cortical extracts. These have varying physiological activity and their exact functions have not yet been determined, but it has been established that **desoxy-**

corticosterone controls the sodium and potassium ionic distribution and that **corticosterone** is intimately connected with carbohydrate metabolism. The cortex also contains ascorbic acid (vitamin C) in the greatest concentration found naturally.

Over-development of the adrenal cortex in children results in **precocious sexual development.** When it occurs in adult females it gives rise to reversion to the secondary sex characteristics of the *male*. There is growth of hair on the face, the complexion becomes coarser and menstruation ceases. The activity of the adrenal cortex seems to be controlled by a hormone secreted by the anterior lobe of the pituitary, called the **adrenotropic principle.**

Pituitary Body or Hypophysis.

The pituitary is a spherical body attached to the base of the brain by a stalk—**infundibulum.** The gland is divided into two lobes, anterior and posterior, separated by an intraglandular cleft. The **anterior lobe** is composed of the *pars anterior*, consisting of masses of epithelial cells and large blood capillaries. Some of the cells have a great affinity for acid stains, others stain strongly with basic dyes; these are known as α and β cells respectively. The **posterior lobe** comprises the pars nervosa and the pars intermedia The *pars nervosa*, the bulk of which is neuroglial cells, is richly supplied with bloodvessels. *Pars intermedia* is composed of basophil cells developed from the pars anterior. Both pars intermedia and pars nervosa contain colloid material which it is believed is derived by secretion from the pars intermedia. Encircling the root of the stalk and spreading on to the base of the brain is the *pars tuberalis.*

The pituitary is credited with exerting a controlling influence over more endocrine organs than any other of the internally secreting glands. To it has been applied the sobriquet, 'The leader of the endocrine orchestra.' From evidence gradually accumulating, however, it seems that the pituitary is itself regulated by factors extraneous to it. The physiological and

the pharmacological actions of the gland have been studied with particular reference to the differentiation in function between the two lobes.

The **anterior lobe** has been credited with the production of a large number of active principles, and although none of them has as yet been isolated in a pure condition, there is considerable evidence to warrant belief in their existence. One of the functions earliest attributed to this lobe was the control of growth. **Hypertrophy**, if it occur before adult

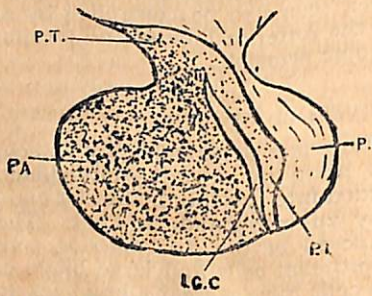


FIG. 60.—DIAGRAM OF PITUITARY BODY. (After Herring.)

P.A., Pars anterior; *P.I.*, pars intermedia; *P.N.*, pars nervosa; *I.G.C.*, intraglandular cleft; *P.T.*, pars tuberalis.

life, gives rise to overgrowth of the skeleton, producing the condition known as **gigantism.** If the excessive secretion occurs after the epiphyses have joined the shafts of the long bones, no increase in stature takes place, but there is a thickening and lengthening of the face bones and of the bones of the hands and feet, accompanied by a "hunching" of the spine. The subject acquires a "bulldog," and sometimes repulsive expression, the condition being known as **acromegaly.** The active principle is known as the **growth hormone,** and if *alkaline* extracts are made of this lobe and injected into suitable animals, increased growth results. The hormone is ineffective by oral administration.

If deficiency of this hormone occur in childhood, the skeleton, although it may be perfectly formed, will be restricted in growth, and an individual thus affected will be a dwarf.

The **thyrotropic** and the **adrenotropic** hormones are two principles which stimulate the thyroid and the adrenal cortex respectively, and these have already been referred to. Two other secretions of the anterior lobe are the **diabetogenic** hormone and the **ketogenic** hormone, both of which are antagonistic to *insulin*. The former raises the glucose content of the blood and the latter facilitates the production of ketone bodies such as hydroxybutyric acid and acetone. It has been shown in a depancreatised dog in which there were present hyperglycæmia, glycosuria and ketonuria, that all these conditions disappeared on the removal of the pituitary. This procedure, however, was not effective in stabilising the carbohydrate metabolism.

Considerable attention has been given recently to the part played by the **gonadotropic** hormones secreted by the anterior lobe. So far, the presence of two has been demonstrated: (*a*) the follicle-stimulating hormone (prolan A), and (*b*) the luteinising hormone (prolan B). **Prolan A** may be obtained from *acid* extracts of the lobe, and when injected into female animals it stimulates the ripening of the ovarian follicles, and thus hastens ovulation. **Prolan B** is found in *alkaline* extracts, and is antagonistic to prolan A. It stimulates the production of corpora lutea, even at the expense of ovulation. Both these hormones are necessary for normal sex development, and if the pituitary is removed this is delayed indefinitely. Alternatively, should hypertrophy occur in childhood, the individual will exhibit sexual precocity.

These hormones are found in the urine of pregnant women, and if such urine is injected into immature female mice it will produce ovulation within five days. This can be readily detected by the appearance of hæmorrhagic spots in the ovaries. This forms the basis of the **Aschheim Zondek** test for pregnancy. **In the male** the gonadotropic hormones stimulate

spermatogenesis and the development of the interstitial gland cells.

Another hormone associated with the physiology of reproduction is **prolactin.** This substance is present in *alkaline* extracts of the anterior lobe, and will initiate and maintain the secretion of *milk* in mammary glands *which have reached a sufficient stage of development.* This is referred to later in the section dealing with the *ovaries.*

The properties of the **posterior lobe** have been investigated mostly by using extracts of the entire lobe. The active principles are supposed to be secreted by the *pars intermedia.* Such extracts affect the blood pressure, the formation of urine, the contraction of the uterus and carbohydrate metabolism. Two definite principles have been demonstrated, vasopressin and oxytocin.

Vasopressin has the effect of stimulating the plain muscle fibres throughout the body. This is particularly manifest in the *arterioles.* The principle acts *directly on the muscle* independent of its nerve supply, and thus differs from adrenaline. The coronary and the pulmonary arterioles are constricted, but the renal and cerebral vessels are dilated. This latter effect is probably passive, due to the general rise in the blood pressure. It also constricts the capillaries. As a result there occurs a **rise in the blood pressure.** This rise is less acute than that obtained from *adrenaline,* but is maintained for a longer period. Although these conditions usually obtain in experimental animals, the effects in *man* are not so uniform. Such injections may even produce a **fall in blood pressure,** although they are always followed by pallor of the countenance due to constriction of the capillaries. After such injections there is a diminution in the rate of formation of urine, even although copious draughts of water may have been imbibed immediately beforehand. This is the **antidiuretic** effect, and whether it is due to the vasopressin or to some other, so far undetected, principle is not yet certain.

Oxytocin has a particular affinity for the musculature of the **uterus,** and its injection is followed by

powerful contractions of the uterine wall. This response to pituitary, however, is not exhibited in the human subject until near the termination of pregnancy.

Injections of the **total extract** of the *posterior lobe*

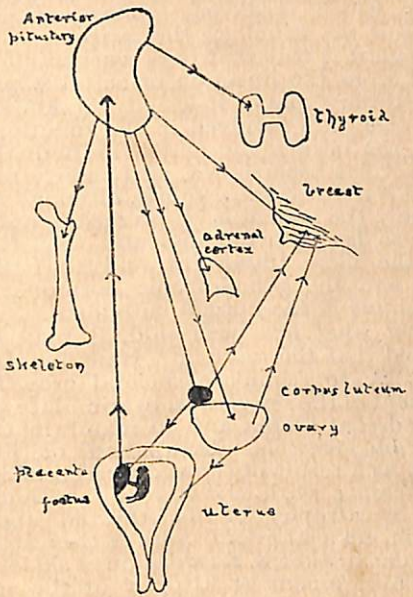


FIG. 61.—SCHEMATIC DIAGRAM TO SHOW SOME OF THE TISSUES CONTROLLED BY ANTERIOR PITUITARY HORMONES, AND THE REGULATION OF THE PITUITARY BY THE PLACENTA.

show not only the effects referred to above, but also a disturbance in **carbohydrate metabolism,** causing hyperglycæmia and glycosuria. Consequent also upon the generalised stimulation of plain muscle which follows these injections the peristaltic movements

of the intestines are stimulated, and there is increased tone in the bladder wall. Sometimes also milk is expelled from the ducts of a lactating mammary gland, but it should be noted that this *expulsion* of milk which may occur is due to the contraction of the plain muscle in the walls of the ducts, discharging the milk which is *already present*. Posterior lobe extract *does not* stimulate the *secretion* of milk.

Although it is true that these various effects may be obtained from the injection of suitable preparations of the pituitary gland, it is not yet known how far some of them are involved in the functioning of the gland in the normal life of the individual. Experimentally it has been shown, particularly in rats, that the gland is not necessary to life, although after hypophysectomy the animal is by no means normal. The evidence so far gathered indicates that the anterior lobe is the more important and that the growth principle and the gonadotropic hormones are functionally active in the normal individual.

Collating what has been said, it may reasonably be assumed that the more important functions of the pituitary are to stimulate skeletal growth and the development of the sex glands, to stimulate the thyroid and the adrenal cortex and to maintain tone in the capillary bloodvessels. **Extirpation** or atrophy of the gland, as a result of the widespread effects following interference with the above functions, will be followed by atrophy of the thyroid and lessened metabolism, emaciation, atrophy of the adrenal cortex and muscular weakness, retardation of skeletal growth, and non-development or atrophy of the sex organs. If the hypofunctioning occur in childhood, the effects will depend upon what parts of the gland are affected, and not only may dwarfism result, but sometimes retardation in mental development and very commonly excessive adiposity.

There is evidence to show that the pituitary is itself subject to control both by nerves and by autacoids. Stimulation of the uterine cervix in the mouse will cause liberation of the gonadotropic hormones; and it has been suggested that the continued secretion

of prolan B during pregnancy is maintained by hormones elaborated in the placenta.

Ovary.

The ovaries, of which there are two, are the distinguishing sex glands of the female. The stroma of the ovary is composed of fusiform cells, and the gland has a covering of cubical epithelium, known as the **germinal layer.** Ingrowths of this epithelium occur and these become detached from the surface. One of the cells in each group so cut off is destined to become an **ovum** and grows larger than the others. The remaining cells increase in number and clustering around the ovum they collectively form a **Graafian follicle.** These cells secrete a fluid—**liquor folliculi,** and during the sexual life of the female it increases to such an amount that the follicle reaches the surface and eventually ruptures. The resultant escape of the ovum and the liquor folliculi into the peritoneal cavity is known as **ovulation.** This is accompanied by a small amount of hæmorrhage into the follicle. The blood coagulates and is absorbed by the ingrowth of cells from the lining layer, which form a yellow structure called the **corpus luteum.** Ovulation occurs about a fortnight after the commencement of the previous menstrual period, and the corpus luteum reaches maturity about five days later. If fertilisation of the ovum does not occur, the corpus luteum degenerates after persisting for a further week, but if pregnancy takes place it increases in size, and functions for the duration of gestation.

There are two internal secretions formed in the ovary, œstradiol and progesterone. **Œstradiol** has been isolated in the chemically pure condition. This was formerly sometimes termed "œstrin." The exact site of its formation in the ovary is not known. It can be obtained from the ovarian tissue or from the liquor folliculi, and it may also be extracted from the liquor amnii and the placenta. An excretion product of œstradiol, **œstrone,** is found in the urine. Both these substances have the same physiological actions,

but œstrone is less potent. Œstradiol is responsible for the development of the uterus and the vagina at puberty, and for the elaboration of the secondary sex characteristics of the female. These include the absence of hair on the face and the development of the breasts. It also causes the hyperæmia and proliferation of the uterine mucosa previous to menstruation, but it does not stimulate the ovaries. **Progesterone,** the active principle of the corpus luteum, has been isolated and its structure determined. This was formerly termed progestin. It is responsible for the efficient embedding of the fertilised ovum in the uterus and the development of the placenta. It inhibits ovulation and menstruation during pregnancy, and it assists in the development of the mammary glands. The removal of the corpus luteum from a pregnant animal will result in abortion.

The **mammary glands** are dependent for their efficient development and function upon at least three hormones. It has been shown experimentally that the injection of **œstrone** causes increased growth of the nipples and proliferation of the ducts. **Progesterone,** either alone or following œstrone, has no effect, but if the two are injected simultaneously there is marked increase in the development of the mammæ. If now **prolactin** (anterior pituitary) is injected, the secretion of milk will commence and will be maintained so long as the injections are continued. In the rabbit all the above phenomena have been observed even after the ovaries have been removed.

Testis.

The testes are the primary sex glands in the male. They are composed of a large number of tubes, the *seminiferous tubules*, between which in the groundwork of the organ are found the *interstitial cells*. The **seminiferous tubules** are lined by several layers of cells which represent various stages in the development of the **spermatozoa.** The latter, when fully formed, are stored in the *vas deferens* and the *seminal vesicles*. Normally the tubules do not commence to function until the age of puberty.

The interstitial cells, sometimes referred to as the **interstitial gland,** diminish in amount after birth until puberty. At this age they increase in quantity, and coincidently the accessory organs of reproduction develop to maturity. The interstitial cells remain constant in amount during the sexual life of the individual, and diminish in old age. They are the likely source of the internal secretion of the testis which determines the **secondary sex characteristics,** amongst which are the deepening of the voice, the growth of hair on the face and trunk and skeletal changes.

Two male sex hormones have been isolated, and their chemical structure determined. One of these, **androsterone,** is found in the urine, the other, **testosterone,** has been obtained from extracts of testicular tissue. The latter is about ten times the strength of the former. When these preparations are injected into castrated animals they stimulate the growth of accessory sex organs, the *prostate* and the *seminal vesicles,* but they have no effect upon the seminiferous tubules. In man, these hormones are secreted continuously throughout the sexual life, and they bear a close chemical relationship to the equivalent hormones secreted by the ovary.

Removal of the testes before puberty prevents the development of all the reproductive organs and of the secondary sex characteristics. If the operation is performed after puberty has been reached there is practically no change either in the health or in the sexual activity of the individual. The absence of the seminiferous tubules will of course render the subject sterile, and it is possible that psychological effects may follow upon the knowledge of having undergone such an operation.

The activity of the testes is controlled by the anterior lobe of the pituitary (*q.v.*). This may be demonstrated by the repeated injection of extracts of this gland; or by grafting transplants of the gland into hypophysectomised animals. Both spermatogenesis and the production of testicular hormones are stimulated, and the latter, if treatment is continued, will

produce overgrowth of the accessory organs of reproduction.

Pancreas.

The pancreas is classed under the endocrine organs in virtue of the internal secretion, *insulin*, which is elaborated in the islets of Langerhans. **Insulin** may be obtained from the pancreas by several methods. One method is to precipitate it, together with the proteins, from pulped pancreas by means of picric acid. The *insulin picrate* may then be dissolved out with acetone, and after recovery this may be converted into the hydrochloride for subsequent use by injection. It is the function of insulin to facilitate the storage of glycogen in the tissues, and to enable them to use glucose. A **deficiency** of insulin in the blood stream will result in hyperglycæmia and glycosuria, the condition being known as **diabetes mellitus.** This may be relieved by the injection of insulin. Should insulin be injected into a *normal* individual, hypoglycæmia will result, and if the dose be sufficiently large, it will be followed by hunger, apprehensiveness, coma and even death. Insulin is destroyed by pepsin and trypsin, and therefore its administration by mouth is valueless therapeutically.

The **secretion of insulin** is continually taking place, the amount varying directly with the quantity of glucose in the blood. The vagus nerves send fibres to the islets, and stimulation of these nerves increases the output of insulin.

The Thymus.

The thymus is not definitely known to be an organ of internal secretion. It is a gland of ectodermal origin in which lymphocytes have collected. It consists of lobes divided into lobules. Each lobule consists of a cortex and a medulla. The cortex is filled with lymphoid cells. The medulla contains only a few lymphocytes, but scattered here and there are the concentric **corpuscles of Hassall.** They possess a hyaline centre and are surrounded by layers of

flattened cells. The thymus increases in size up to puberty and then undergoes involution. It also wastes in starvation and in vitamin-B deficiency.

The function of the thymus is still under investigation. It has long been assumed that a relationship existed between the thymus and the gonads, but most experiments designed to demonstrate this have given conflicting results. Quite recently, however, it has been shown that if extracts of thymus are injected into rats for about a fortnight, and if similar treatment be applied to the successive generations of such rats, there will result a progressive acceleration in development of size and sexual maturity. In one such experiment the rats of the ninth generation were born with a hair covering; the testes descended and the vagina opened in a few days, and they became pregnant at three weeks. In the control rats hair did not appear until they were two weeks old; descent of the testes occurred seven weeks, and pregnancy twelve weeks, after birth.

The Spleen.

The spleen is primarily concerned with the disposal of the formed elements of the blood, but so far as is known does not produce any autacoid substance. It is invested by peritoneum, and is enclosed in a fibrous capsule containing plain muscle, which sends a network of processes—trabeculæ—into the interior of the gland. The smaller arteries are surrounded by small masses of lymphoid tissue, which appear as rounded structures on section, and are termed the **Malpighian corpuscles** of the spleen. The rest of the organ consists of **reticulo-endothelial tissue,** the interspaces of which are continuous with the splenic arterioles and the commencement of the splenic veins, so that they are filled with blood. The whole of this tissue, with the blood it contains, is called **splenic pulp.**

In virtue of the reticulo-endothelial tissue which is highly developed in the spleen, this organ is one of the important sites in the body where red blood corpuscles are broken down. The iron is removed from

the hæmoglobin and stored in the spleen, and the residue of the pigment is converted into bilirubin and is carried by the splenic vein to the portal circulation. In post-natal life the spleen takes no part in the *formation* of red blood corpuscles except during anæmia or after severe hæmorrhage.

The splenic pulp acts as a **reservoir** for blood, and here the red blood cells are held in greatest concentration. In emergencies such as muscular exertion, hæmorrhage, oxygen want or carbon monoxide poisoning, the spleen is contracted and further supplies of red cells are passed into the circulation. This the spleen is able to do in virtue of the plain muscle which forms part of its structure. These muscle fibres are innervated by the sympathetic nerves.

Extirpation of the spleen is not fatal to life, and in many instances no detrimental effects are noticeable. Splenectomy is followed by a marked rise in the platelet count, and also the red cells usually become less fragile. It has been observed, however, that a subject on whom splenectomy has been performed has a lowered resistance to bacterial infection, and evidence has been obtained indicating that one of the functions of the spleen is to manufacture bacterial antibodies.

CHAPTER XIX

REPRODUCTION

In order that the propagation of the species may continue, it is essential in man that both sexes contribute to the formation of the new generation. In the female there are developed the ova, limited in amount, and in the male the spermatozoa in countless millions. The conjugation of one sperm with one ovum marks the beginning of a new individual.

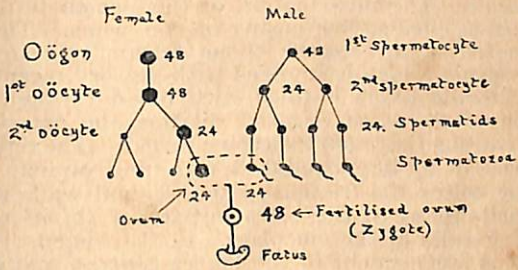


FIG. 62.—SCHEME SHOWING MATURATION OF THE OVUM AND THE SPERMATOZOON, AND FERTILISATION OF THE OVUM.

The figures indicate the number of chromosomes at each stage.

The ovum is developed from one of the cells of the germinal layer of the ovary. In the human subject this cell contains 48 **chromosomes,** and before it becomes ready for fertilisation it undergoes a series of changes whereby it loses half its number of chromosomes. This is known as **maturation of the ovum.** The process is diagrammatically shown in Fig. 62. In due course the ripe ovum escapes into the peritoneal cavity from the ruptured Graafian follicle and finds its way by the fimbriated extremity into the Fallopian tube.

The spermatozoa are developed in the seminiferous tubules of the testes, and, like the ova, they are

derived from the primordial germ cells. Here also the process of maturation has to take place whereby in the ripe spermatozoa there are only 24 chromosomes. The fully formed spermatozoa possessing a head and a relatively long tail are now stored in the epididymis, the vas deferens and the seminal vesicles. In man, as in all mammals, it is necessary for the spermatozoa to be implanted in the female, and to facilitate this they are suspended in a nutrient and lubricating fluid contributed to by the testes, seminal vesicles, prostate and Cowper's glands. The combined fluids and the suspended sperms are known as *semen*. The introduction of this semen into the female is effected by means of the penis. This is composed of an erectile tissue terminating in the glans penis, which is supplied with sensory receptors. The erectile tissue is filled with blood through the action of the *nervi erigentes* dilating the arterioles, thus causing the organ to become turgid. The rigidity enables it to be introduced into the vagina, and during coitus the friction of the vaginal walls upon the end-organs in the glans initiates a *spinal reflex* which results in the ejaculation of the semen. This reflex is independent of the higher centres, and may occur after section of the cord in the mid-dorsal region. It has been calculated that upwards of 100,000,000 sperms are implanted at each ejaculation. Most of the spermatozoa do not survive for long, but some, more active than the rest, enter the opening into the uterus, the *os uteri*, and in virtue of their flagellæ propel themselves forwards along the *cervix* and into the cavity of the uterus. Eventually they reach the openings of the Fallopian tubes along which they pass, and if an ovum should be present, **conception** takes place by the entry into the ovum of *one* spermatozoon. This combination of an ovum with 24 chromosomes and a sperm with 24 chromosomes yields a *zygote* with the full complement of 48 chromosomes. Segmentation now commences immediately by the usual process of karyokinesis, so that each subsequent daughter cell produced contains 48 chromosomes. During this division the ciliated epi-

thelium lining the Fallopian tube is gradually propelling the fertilised ovum, now a mass of cells known as the *morula*, into the uterus where it becomes implanted. Some of the cells are destined to form the embryo, others to function in looking after its nutrition. The latter eventually form a structure called the **placenta**, which burrows its way by means of processes called *chorionic villi* into the *decidua*, which is a development of the uterine mucosa, rich in blood sinuses. By this arrangement facilities are provided for the free interchange of dissolved substances between the maternal and fœtal bloods, but the two circulations never come into direct contact with each other. It has been shown that at least in some mammals the hydrogen ion concentration of the maternal blood in the later stages of pregnancy is higher than that of the fœtal blood. This will have the effect of facilitating the transference of oxygen from the maternal blood to the fœtus, and of CO_2 from the fœtus to the mother. The fœtus is connected to the placenta by means of the **umbilical cord**, which carries two arteries and one vein. The arteries convey venous blood to the placenta; the vein brings back arterial blood to the fœtus.

The fœtal circulation calls for special comment. The umbilical vein enters the portal vein near the liver but also connects with the inferior vena cava by means of the *ductus venosus*. The bulk of the arterial blood enters the vena cava and is carried to the right atrium. Here, because of the Eustachian valve, it is diverted into the left atrium through the *foramen ovale*, an opening between these two atria which exists only in the fœtus. The blood now passes into the left ventricle and thence via the aorta to be distributed to the head and the rest of the body. The blood return from the head and upper extremities enters the right atrium and passes through into the right ventricle. From here it leaves by the pulmonary artery, but as the lungs are not functioning it is short-circuited into the aorta through the *ductus arteriosus*, another fœtal structure situated distal to the bloodvessels supplying the brain and

upper extremities. The only arterial blood in the fœtal circulation is that in the umbilical *vein*, but it will be observed that in the above scheme the purest

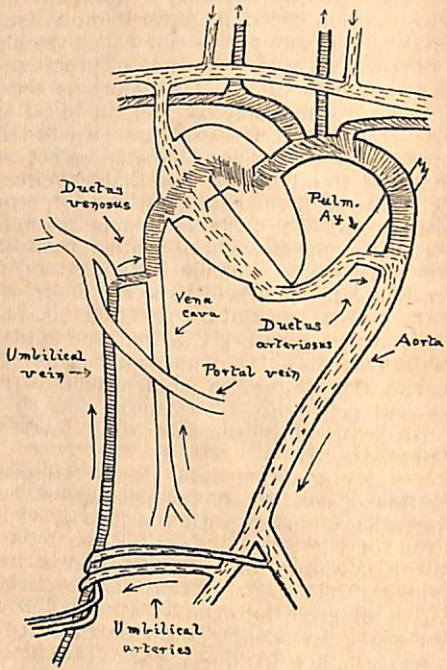


FIG. 63.—SCHEMATIC DIAGRAM OF THE CIRCULATION IN THE FŒTUS (*see* TEXT).

blood is sent to the brain and upper extremities, the less pure blood being diverted to the rest of the body.

While the fœtus is developing, the uterus is increasing in size to accommodate it, and during this time the uterine capacity may be enlarged 2,000 times.

Throughout gestation the uterine walls exhibit slow rhythmic contractions, and at the end of this period, about 40 weeks after fertilisation, these contractions become more powerful until finally the fœtus is expelled. This is known as **parturition.** The factors which determine this period are not known, but it has been demonstrated that at this time the uterine muscle shows a maximum sensitivity to the action of *oxytocin.* After the birth the umbilical cord is ligatured and this procedure causes the fœtal blood to become venous. The combined effect of this venous blood and the stimulus of the cold air upon the child stimulate the respiratory centre and so cause an inspiratory movement to be taken. Respiration now proceeds and the child commences a separate existence. Usually a definite interval elapses between the delivery of the child and the expulsion of the placenta, or afterbirth. In a few days the ductus venosus and the ductus arteriosus are obliterated, in a few months the fenestra ovalis closes, and the circulation of the blood pursues its normal course.

THE HUMAN SEXUAL CYCLE. — In man and in monkey the sexual cycle is characterised by the occurrence of the menstrual flow. This bears a certain relationship to changes which are occurring in the ovaries, and they are believed to be as follows:

During the reparative and resting stages (ten days), a Graafian follicle is in the process of developing, and reaches maturity about fourteen to fifteen days after the beginning of the last menstrual period. The ovum is now shed, and at this stage the glands in the uterine mucosa begin to enlarge and secrete mucus; concurrently the formation and development of the corpus luteum is proceeding. Gradually the underlying layers lining the uterus become more and more suffused with bloodstained lymph, and about fourteen days after ovulation there is a breakdown of the superficial epithelium and rupture of blood capillaries. This debris of epithelium, blood and mucus then escapes from the uterine cavity and constitutes the menstrual flow, which lasts for about five days. If

the ovum is not fertilised, the corpus luteum atrophies, another Graafian follicle ripens and the cycle is repeated. This may be graphically represented as follows:

10 days	13 days	5 days
Reparation →	Congestion → Breakdown →	Menstruation
	Ovulation	
	Corpus luteum formed →	Atrophy C.L.

Although the above relationship is believed to hold, it must be noted that menstruation may occur in the absence of ovulation. Also it has been shown that in ovariectomised women the menstrual flow may be induced by the injection of œstrone followed by progesterone.

Sexual Cycle in Lower Mammals.—In many of the lower mammals the sexual activity is limited to certain periods in the year known as the breeding season. During this time changes occur in the ovary and uterus known as the **œstrus cycle.**

In the non-breeding season the ovary is quiescent, the uterus is thin and anæmic and the animal exhibits no sexual desire. This is the period of **anœstrus.** During the breeding season the œstrus cycles occur, beginning with the condition of **pro-œstrus,** in which development of the Graafian follicles takes place accompanied by congestion in the uterus and hypertrophy of the vagina. This is succeeded by the period of **œstrus,** the only stage at which the animal will accept the male, or in which it is fertile. During this time ovulation occurs, and if copulation takes place and the conditions are favourable, the animal becomes pregnant. In the *rabbit* ovulation does not occur until after copulation.

If pregnancy does not take place, the conditions subside, known as **metœstrum,** and after an interval which varies with the species the cycle is repeated. In those animals in which there is no particular breeding season there is no period of anœstrus.

TABLE OF VITAMINS.

Vitamin.	*Source.*	*Effects of Deficiency.*	*Approximate Daily Needs.*	*Stability.*
A Axerophthol ($C_{20}H_{29}OH$). Fat-soluble.	Animal fats: fish liver oils, butter, egg yolk—and as carotene in vegetables, spinach.	Keratinisation of epithelium of conjunctiva and hollow viscera. Night blindness.	2 mg. (6,000 Int. Units).	Readily oxidised.
B_1 Aneurin Thiamin chloride ($C_{12}H_{17}N_4SOCl.HCl$). Water-soluble.	Silver husks and embryos of cereals; yeast, liver, egg yolk.	Loss of appetite, constipation, neuritis, beri-beri.	1·5 mg. (500 I.U.).	Destroyed by excess heat and by alkalies.
B_2 (*a*) Riboflavin ($C_{17}H_{20}N_4O_6$). Water-soluble.	Yeast, bran, milk, liver, kidney.	Growth retarded. Carbohydrate oxidation impaired.	3 mg. (no I.U.).	Resists heat but labile to alkalies and sunlight.
(*b*) P-P factor. Nicotinic acid (C_5H_4NCOOH). Water-soluble.	Yeast, liver, milk, meat, egg.	Pellagra, acrodynia, sprue.	Therapeutic, 50-100 mg.	Very stable.

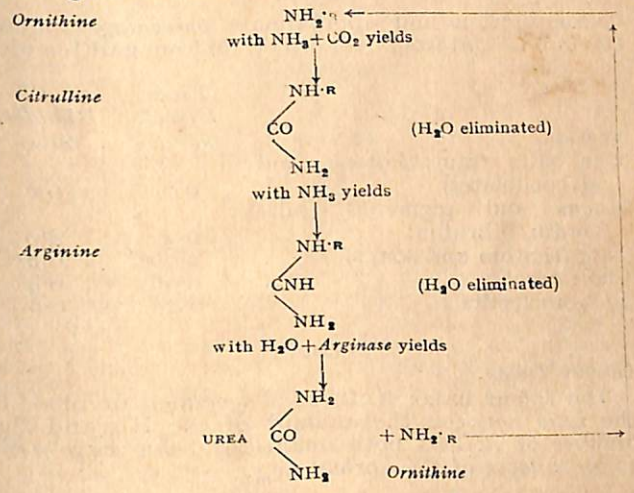
TABLE OF VITAMINS—*continued.*

Vitamin.	*Source.*	*Effects of Deficiency.*	*Approximate Daily Needs.*	*Stability.*
C *l*-Ascorbic acid ($C_6H_8O_6$). Water-soluble.	Fresh fruits: oranges, lemons, tomatoes; turnips, green vegetables.	Tissue oxidations, bone and R.B.C. formation impaired. Capillary hæmorrhages, scurvy.	60 mg. (1,200 I.U.)	Easily oxidised unless kept in acid medium.
D_2 Calciferol ($C_{28}H_{43}OH$). Fat-soluble.	Irradiated ergosterol.	Ca and P absorption impaired. Rickets, dental caries.	·012 mg. (500 I.U.)	Very stable; withstands cooking.
D_3 ($C_{27}H_{43}OH$). Fat-soluble.	Animal fats, fish liver oils, irradiated milk.	Ditto.	Ditto.	Resists heat; not readily oxidised.
E Alpha-tocopherol ($C_{29}H_{50}O_2$). Fat-soluble.	Wheat germ, lettuce, egg yolk, milk.	Degeneration of germinal epithelium. Sterility, abortion.	5 mg. (5 I.U.)	Easily oxidised; withstands heat.
K 2-methyl-1,4-naphthoquinone *et var.*	Alfalfa, pig liver fat. Green vegetables, soybean	Reduced coagulability of the blood. Hæmorrhages.	Therapeutic, about 5 mg.	

Formation of Urea from Arginine.

It has been shown that in the liver NH_3 and CO_2 can combine with ornithine to form arginine. This in the presence of the enzyme *arginase* is hydrolysed into UREA and ornithine, and the latter is again free to repeat the cycle.

Ornithine, di-amino valeric acid, possesses the formula $NH_2 \cdot CH_2CH_2CH_2CHNH_2COOH$. This may conveniently be represented as $NH_2 \cdot R$, and the cycle of changes shown as follows:



Liver.

The following are amongst the functions of the liver:—

Deaminises unwanted amino acids, and forms urea from the amino groups liberated.

Converts into glycogen the excess monosaccharides absorbed from intestine, and reconverts it back again into glucose when required.

Desaturates the larger fatty acids so that they can be more readily oxidised.

Detoxifies products of putrefaction—*e.g.*, indole and skatole, absorbed from large intestine.

Manufactures fibrinogen, an essential for the clotting of shed blood.

Manufactures heparin, which prevents the clotting of blood in the bloodvessels.

Manufactures bile.

Bile.

Composition and approximate *percentage* quantities of bile—(*a*) from liver direct, (*b*) from gall-bladder.

	Liver Direct.	*Gall-Bladder.*
Water	98·0	89·0
Bile salts (taurocholates and glycocholates)	0·7	6·0
Mucus and pigments (biliverdin, bilirubin)	0·4	3·0
Fats (lecithin and soaps) ..	0·06	0·8
Cholesterol	0·06	0·4
Inorganic salts	0·8	0·8

Blood.

Colour Index.

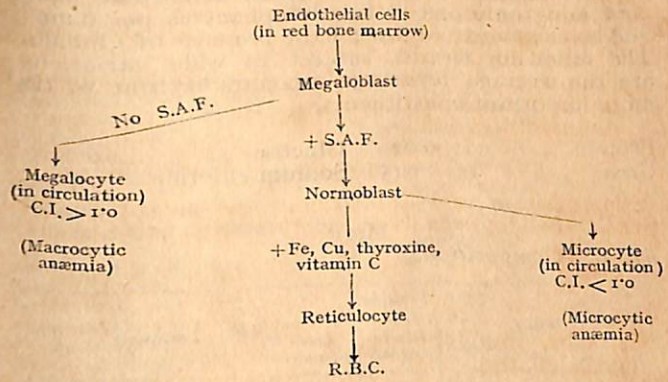
The colour index (C.I.) of a specimen of blood is the *ratio* between the amount of the Hb and the number of R.B.C., both quantities being expressed as *percentages* of the normal—*e.g.*:

$$\frac{\text{Hb } 86 \text{ per cent.}}{\text{R.B.C. } 90 \text{ per cent.}} = \text{C.I. } 0{\cdot}95.$$

Formation of Red Blood Corpuscles.

For the efficient manufacture of R.B.C., there must be present, in addition to other building materials, the specific anti-anæmic factor (S.A.F.), Fe, Cu, thyroxine and vitamin C. The following *schema* shows the genesis of a R.B.C., and the deviations

from the normal which occur if certain of the above substances are deficient in amount.



Specific Anti-Anæmic Factor (*S.A.F.*).

This substance is formed by the combination of an *extrinsic* factor, found in beef and yeast, and an *intrinsic* factor, hæmopoietin, found in the gastric mucosa. It is stored in the liver, and its formation cannot occur if there is an absence of hydrochloric acid in the gastric juice.

Blood Plasma.

The following are the more important constituents found in blood plasma. Average *percentage* values are given, but some of these—*e.g.*, glucose—vary widely in amount within the physiological range.

Albumin	5·0	Sodium chloride	0·5
Globulin	2·0	Potassium	0·02
Fibrinogen	0·3	Calcium	0·01
Glucose	0·1	Phosphorus	0·005
Urea	0·03	Magnesium	0·0025
Creatinine	0·001		

Cerebrospinal Fluid.

Cerebrospinal fluid is a clear, colourless liquid containing only one or two lymphocytes per c.mm., and gives a negative test for the presence of globulin. The following figures, subject to wide variations, are the average *percentage* amounts present of the more important constituents.

Protein ..	.. 0·02	Glucose ..	.. 0·07
Urea ..	.. 0·025	Sodium chloride	0·7

Milk.

Average Composition.

	Water.	*Proteins.*			*Fat.*	*Lactose.*	*Inorganic Salts.*
		Total.	*Caseinogen.*	*Lactalbumin.*			
Cow	87	3·5	3·0	0·5	3·5	4·8	0·8
Human	88	1·5	0·5	1·0	3·5	6·5	0·2
Goat	86	4·3	—	—	4·6	4·2	0·8

Urine.

Average quantity of urine and its constituents passed in twenty-four hours by a normal human adult. These quantities may be subject to wide variations depending upon the work done and the food eaten.

	Total.	*Per Cent.*
Volume	1,500 c.c.	—
Urea	30 g.	2·0
Sodium chloride	15 g.	1·0
Sulphur	2·5 g.	0·16
Phosphorus	2·5 g.	0·16
Ammonia	1·0 g.	0·07
Creatinine	0·9 g.	0·06
Hippuric acid	0·5 g.	0·04
Uric acid	0·5 g.	0·04

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